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THE ELECTRICAL REACTIONS OF MUSCLES BEFORE AND AFTER NERVE INJURY.

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WHEN the nerve leading to a muscle is damaged or destroyed, the muscle shows in its response to the electric current a series of changes which are grouped together under the name "reaction of degeneration." These changes may be classed conveniently under two heads: (1) changes in the character of the electric current required to excite the muscle; and (2) changes in the response of the muscle to excitation. The changes in the response consist in the reduced rapidity, slow subsidence and weak power of the contraction, and sometimes in its localization to the neighbourhood of the electrodes. These suffice to give a rough idea of the state of the muscle, but it is very doubtful if the most exact measurements of them would give information which could be regarded as quantitative, since they depend not only on the degree of degeneration, but also on such transitory conditions as the temperature of the limb, whether it has been massaged recently or not, &c.

In regard to the changes classed under the first head, the position seems more hopeful, and in recent years more and more stress has been laid on the measurement of the current required to excite, as giving a true indication of the state of the muscle and its nerve. It is the purpose of the present inquiry to find out if possible more exactly the relation between the state of the muscle and the nature of the current required to excite it, to investigate the causes underlying this relation, and to see how much diagnostic information may be gained by the different methods at present in vogue.

In the ordinary method of testing with faradic and galvanic currents,

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the stimulus may be varied at will as regards its strength but not as regards its duration. The faradic current rises rapidly to its maximum in about 0·0001 second (the exact constants depending on the dimensions of the coil) and falls more slowly to zero. In practice the current is repeated many times a second, but this is simply a matter of convenience, as it allows the contraction to be more easily observed—the muscle responds as readily to a single shock as it does to a series of shocks. The galvanic current rises instantaneously to its maximum value and remains at the same level until it is turned off. Without special apparatus its duration cannot be controlled if it is much less than $\frac{1}{2}$ second, and if it is greater than this its duration makes no difference to the efficacy of the current. Thus we are confined to a very brief current and a very long one, and there is nothing between the two. With this arrangement it is easy to tell whether the nerve to a muscle is damaged or not, since a muscle with intact nerve supply will respond to the brief faradic current, whereas one with a damaged nerve supply will not respond to this, but will respond to the longer galvanic current. However, this information is entirely qualitative, and it does not allow us to make any estimate of the exact state of affairs. Some additional information may be gained from the alterations in the strength of the current required to excite, but unfortunately such changes may be due to altered skin resistance, increase of fluid in the subcutaneous tissues, &c., quite apart from any change in the condition of the nerve supply. At the same time, it is clear that the degeneration of the nerve causes an increase in the duration of the current required to excite the muscle, and this suggests that if we could measure the least effective duration it might give valuable quantitative information about the condition of the muscle and nerve.

For this purpose the method of condenser discharges has been introduced by Cluzet [1] in France and Lewis Jones [3] in this country. This method depends on the fact that the discharge of a condenser through a constant resistance varies in duration according to the capacity of the condenser. The discharge starts at its maximum value and falls off gradually, and with the sets of condensers in use at present it is possible to obtain currents whose total duration varies from 0·00004 second to 0·005 second. By inserting special resistances even longer discharges may be obtained. With these currents it is found that the more severe the injury to the nerve appears to be, the greater is the capacity of the condenser (and therefore the longer is the duration

of the discharge) required to excite the muscle. Thus the method would seem to give all the information which could be desired from a clinical point of view: we have only to find the least capacity of condenser which will excite the muscle, and this will give a measure of the severity of the injury. Unfortunately, the principles which underlie this method have never been thoroughly decided, and the conclusions which are based on it are derived almost entirely from observations on the human being, and very little from experimental work on animals or on isolated muscle and nerve preparations. Indeed, two years ago Laugier [5] pointed out that a consideration of the facts which are known in regard to the electrical stimulation of cold-blooded tissues shows that there is a serious fallacy in the condenser method as it is used at present. These facts are stated briefly in the following section.

The Relation of Current Strength to Current Duration in Cold-blooded Tissues.

Within the last ten years the precise conditions under which an electrical current will stimulate the excitable tissues of cold-blooded animals have been worked out with some approach to certainty. The relations between the condition of the tissue, the form of the current, its strength and its duration have been studied exhaustively and reduced to mathematical terms by Keith Lucas [7], Lapicque [4], A. V. Hill [2], and others, and though there is still some difference of opinion as to the theoretical interpretation of these relations, their exact form is no longer in doubt. The most fruitful results have been obtained by the use of constant currents, that is, of currents whose strength rises immediately to a fixed value and remains at that value as long as the current is flowing. In such currents there are only two variables to consider, the strength and the duration, and both of these are easily controlled. When these currents are applied to a simple tissue, such as the sciatic nerve of the frog, it is found that currents of less than a certain minimal duration will not excite, however strong they may be; with longer currents the strength required to excite becomes less and less as the duration increases, until eventually it falls to a constant level which cannot be reduced further by increasing the duration. This relation is shown in fig. 1, which is constructed from an experiment by Keith Lucas [6] on the sartorius muscle of the toad. In this case, however strong the current may be it will not excite at all if its duration is less than 0·003 second. With slightly longer durations a

very strong current is needed, and the strength falls off gradually as the duration is increased. Eventually the minimal strength is reached, and when the potential difference is less than 0·076 volt the current will not excite, however long its duration may be. Thus the current which will excite the muscle must possess a duration longer than 0·003 second and a strength greater than that given by 0·076 volt. In between these limiting values the relation between strength and duration is expressed by a curve which is convex to the origin.

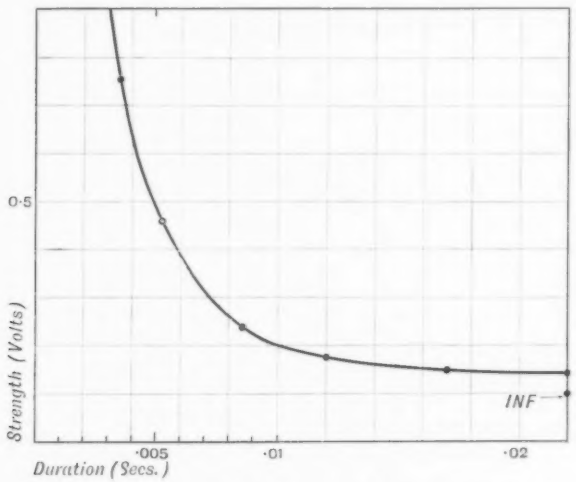

FIG. 1. Relation between strength and duration of current required to excite the sartorius muscle of the toad. (Keith Lucas.)

A curve which is almost identical with fig. 1 is found for every preparation of the toad's sartorius, the only difference being that the minimal current strength required to excite will naturally depend on the resistance of the muscle, the dimensions of the electrodes, &c. In every case the current required to excite begins to increase when the duration is reduced much below 0·02 second, and is doubled when the duration is about 0·01 second. This holds good for the sartorius of the frog as well as that of the toad, and for the gastrocnemius as well as the sartorius. A curve of the same form is given by the sciatic nerve of the frog or toad and by the nerve-fibres in the substance of the muscles, but in this case the time-factor is much less important and the minimal strength does not begin to rise until the duration is less

than about 0·003 second. Ventricular muscle shows a much slower reaction than voluntary muscle, the minimal strength rising at about 2·0 seconds. In every case which has been examined (and this includes the muscles and nerves of a variety of cold-blooded animals) the curve is of the same form, and is approximately constant for similar tissues under similar conditions.

Various equations have been found to fit the curve. That of Weiss [12] is the simplest and that of A. V. Hill [2] conforms most accurately to the experimental results. Weiss's equation is:—

$$i = a + bt,$$

where i is the current strength, t the duration, and a and b are constants. Hill's equation is:—

$$i = \frac{\lambda}{1-\mu\theta^t}$$

where λ, μ and θ are constants. The constants are easily calculated in either case, and in Hill's equation they are given a definite physical interpretation. However, for all practical purposes the curve may be defined by two factors, one of which is the least current required to excite at infinite duration, and the other a time-factor depending on the "rapidity" of the tissue. This factor is given approximately by the duration at which the current strength must be doubled, a quantity which is equal to the ratio $\frac{a}{b}$ in Weiss's equation. Lapicque has proposed the name "chronaxie" for this quantity, and his nomenclature will be adopted in the following discussion. It follows, then, that for any given tissue a determination of the duration at which the current strength must be doubled suffices to fix the strength-duration curve for that tissue.

The characteristics of this curve have been insisted on at some length because of its great importance in connexion with electrodiagnosis. In the first place, it is clear that the least duration which a current must possess if it is to stimulate the excitable tissues of a cold-blooded animal depends not only on the nature and condition of the tissue, but also on the strength of the current. A strong current will excite at very much shorter durations than a weak current. The same holds good for condenser discharges as for constant currents, and therefore the least effective duration of a condenser discharge will depend on the strength of the discharge as well as on the state of the tissue to which it is applied, and if the excitability of the tissue happens to change, the least effective duration corresponding to a given

strength of current will change too. If the same reasoning can be applied to mammalian muscles and nerves, it is clear that the method of condenser discharges cannot give a true indication of the state of affairs unless precautions are taken that the strength of the discharge shall always bear the same relation to the strength required when the duration is infinitely long. In the ordinary condenser method this precaution is not taken, and Laugier's criticism of the method rests on this ground. Clearly, then, to make sure that this objection is valid it is important to find out how far the relation expressed in Weiss's or Hill's equation is true for mammalian as well as for cold-blooded tissues.

The determination of the strength-duration curve is important for another reason. In the cold-blooded tissues the time factor of the curve, the "chronaxie," is constant for similar tissues examined under similar conditions, and differs greatly from one tissue to another. Thus the determination of the curve makes it possible to distinguish clearly the nature of the tissue upon which the stimulus takes effect. For instance, it is possible to tell whether the current applied to a muscle stimulates the muscle-fibres directly or indirectly through the medium of the intramuscular nerve-fibres. The value of this will be seen hereafter.

The Relation between Current Strength and Current Duration in Healthy Muscles.

The apparatus required for the determination of the strength-duration curve in human subjects must be capable of delivering a constant current varying in duration from $\frac{1}{10000}$ second to $\frac{1}{10}$ second and at a potential varying from 1 to 100 volts or more. In practice the duration was controlled by a Lucas pendulum [10], and the potential by a potentiometer connected to the 200-volt mains (continuous). The potentiometer consisted of two dial resistance boxes, the resistance in the two together being maintained at a constant value of 1,000 ohms. The current was led off from the potentiometer through a 500-ohm resistance to the stimulating electrodes. This resistance was inserted to cut down the current which would otherwise pass when the short-circuit key, K_1, is closed. In the circuit from the potentiometer were two knock-down keys, one in the circuit through the patient and the other in a short circuit which avoided the patient and returned the current direct to the potentiometer. The two keys were opened by means of the pendulum, and the interval separating their opening could be varied from 0·0001 second to 0·2 second. The arrange-

ment of the connexions is shown in fig. 2. The resistance boxes are lettered **A**, **B**, and **C**, and the keys K_1 and K_2. When the short-circuit key, K_1, is opened by the pendulum, the current begins to flow through the patient, and when the in-circuit key K_2, is opened, the flow ceases. By altering the ratio of the resistances in the two halves of the potentiometer, the potential difference between the points **A** and **B** can be varied from 1 to 200 volts. Thus both current strength and current duration can be varied within fairly wide limits. The whole arrangement is practically identical with that devised by Keith Lucas [9] for use in his experiments on cold-blooded tissues. No attempt was made to measure the current directly; this is not essential, since all we require to know is the strength compared with that required to excite when the duration is infinitely long; furthermore, it is impossible to measure the strength without using a ballistic galvanometer or some such method, since the currents are too short in duration to affect the usual measuring instruments, and too strong to be borne comfortably by the patient if they are allowed to run for any length of time.

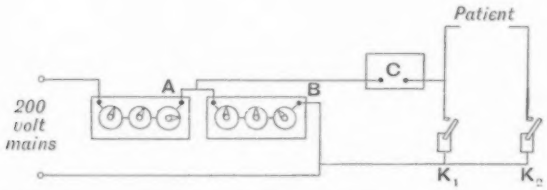

FIG. 2.—Apparatus for delivering constant currents of variable strength and duration.

In the following experiments the current strength is always expressed as a multiple of that required to excite when the duration lasts for several seconds. This is given the value 10, and is spoken of as the strength at infinite duration, for when the duration exceeds one or two seconds its exact value is found to make no difference to the strength.

The majority of experiments to be described were made on the tibialis anticus muscle. This is an ideal muscle for the purpose as it is easily excited and its contractions are easily observed and distinguished from those of neighbouring muscles. Moreover, it is frequently paralysed in injuries of the sciatic, poliomyelitis, &c. In working with this muscle a large pad electrode was placed under the calf to serve as the anode, and a small pad, 1 in. square, was bandaged on to the front of the leg for the kathode. The exact position of this was found to be

unimportant, but as a rule it was secured with its centre 1 in. from the anterior border of the tibia and 2 in. below the level of the head of the fibula. Both electrodes were soaked in a solution of ammonium chloride. With this arrangement the strength of current required to excite at infinite duration does not vary by more than 5 per cent. during a series of measurements lasting twenty minutes or more. The contraction of the muscle is best detected by placing the index-finger across the surface of the muscle with its tip resting on the border of the tibia. The contraction of those fibres lying immediately external to the tibia can be felt by this method when their contraction is too weak to produce any movement of the foot or any visible deformation of the skin.

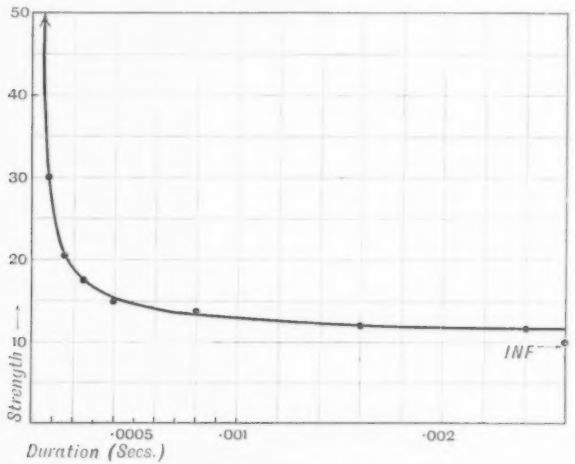

FIG. 3.—Strength-duration curve for human tibialis anticus with intact nerve supply.

The strength-duration curves were always determined in the following way: First of all the current was made and broken after an interval of some seconds by a hand switch, and the potentiometer was adjusted so that the current was just strong enough to produce a contraction. This gave the strength at infinite duration. If this appeared to be constant after several measurements, the pendulum was set to give a current lasting for about 0·1 second, and the requisite strength was redetermined. The duration was reduced still further and the strength required to excite was determined for each duration, until eventually the duration was so short that currents five or six times the value at infinite duration failed to excite the muscle. The duration was then

increased to check the previous results, and, finally, the strength at infinite duration was determined again. As a rule, the results of the two sets of readings with the duration decreasing and increasing agree very well, the difference in two readings at the same duration being rarely greater than 5 per cent., and usually less.

A typical curve for the tibialis anticus with intact nerve supply is shown in fig. 3. In this and in all subsequent figures the current strength is shown by the ordinates, the strength at infinite duration being given the value 10, and other strengths expressed as multiples of this. The duration of the current is shown by the abscissæ. In the present case it will be seen that the curve rises very gradually until the duration is reduced to about 0·0003 second. As the duration is reduced still further, the curve rises very rapidly, and at 0·0001 second a current over three times as strong as that at infinite duration is required to produce a contraction. As the significant durations are so short and the probable error is large, it is difficult to be certain as to the precise form of the curve, but the current strength appears to be doubled at a duration of about 0·00018 second. Thus the chronaxie in this case is 0·00018 second. A value which varies between 0·00025 second and 0·00008 second was found in all the healthy muscles examined, and this holds good not only for the tibialis anticus, but for all the other muscles which were investigated—the biceps, the flexors and extensors of the forearm, the extensors of the thigh and the small muscles of the thumb.

The actual values of the chronaxie for healthy muscles in six different individuals are shown in Table I. When the kathode is applied to a nerve-trunk instead of to a muscle, the chronaxie is on the whole slightly longer. In the case of the external popliteal nerve the average of four determinations gave 0·00025 second. However, the measurement is more difficult than in the case of a muscle, and for this reason the difference cannot be insisted upon.

TABLE I.—Chronaxie of Muscles with Intact Nerve Supply.

Muscle	Subject	Chronaxie
Tibialis anticus	a ..	0·00016 second.
,, ...	b ..	0·00008 ,,
,, ...	c ..	0·00015 ,,
,, ...	d ..	0·00025 ,,
,, ...	e ..	0·00016 ,,
Biceps	a ..	0·00012 ,,
,, ...	b ..	0·00020 ,,
Extensor longus digitorum ..	b ..	0·00024 ,,
,, ,, ..	e ..	0·00010 ,,
Tensor fasciæ femoris ..	a ..	0·00008 ,,
,, ,, ..	b ..	0·00015 ,,
Average value for all muscles	.. ..	0·00016 ,,

The Strength-duration Curve in Denervated Muscles.

The simplest case to consider is one in which there has been a complete section of the nerve, the muscle being examined at a time when all the nerve-fibres peripheral to the injury must have degenerated and before there are any signs of recovery. The observations to be recorded in the present section were made on the tibialis anticus at different times after the section of the sciatic or external popliteal nerve. Records were made from four patients showing the syndrome of complete sciatic division (due to gunshot wounds), and in three of these the division of the nerve was verified by operation. The fifth case is one of injury to the external popliteal. The following is a short summary of the cases :—

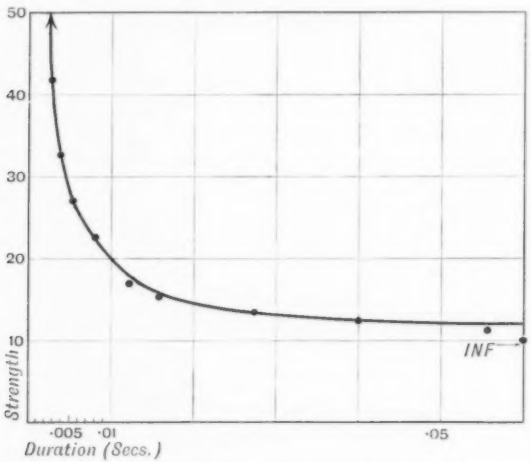

Fig. 4.—Tibialis anticus six months after division of sciatic.

Case 1.—The patient was shot through the right leg on March 10, 1915. There was complete paralysis of all the muscles below the knee and complete sensory loss over the area supplied by the sciatic. There was no pain and not much wasting of the muscles. Tested in the ordinary way, the tibialis anticus showed the complete reaction of degeneration. As there were no signs of recovery, the sciatic was exposed on October 30, 1915, and it was found to be completely divided, with a gap of $2\frac{1}{2}$ in. between the ends. Fig. 4 shows the strength-duration curve determined on September 28. The curve is of the same form as that in figs. 1 and 3, but the slope is much more gradual, and the current strength is doubled at 0·0095 second and increased to five times the threshold

value at 0·0027 second. Thus the chronaxie is 0·0095 second. In the other leg, which was uninjured, the tibialis anticus gave a chronaxie of 0·00012 second, the usual value for muscle with intact nerve supply. Thus the chronaxie of the denervated muscle is nearly 100 times as long as that of the corresponding healthy muscle. The determination was repeated on December 4, nearly two months after the operation and three months after the first determination. The curve coincides within the limits of error with the earlier determination, the chronaxie being 0·011 second.

Case 2.—In this patient the left sciatic was wounded in March, 1915, and a month later the wound was opened and a portion of the nerve which had been converted into scar tissue was removed and the ends of the nerve were sutured. There was the usual motor and sensory loss, and there were no signs of recovery when he was examined. The curve was determined on September 17, 1915, and again on September 30. In both cases the chronaxie was 0·011 second and the curves were almost identical with those in Case 1.

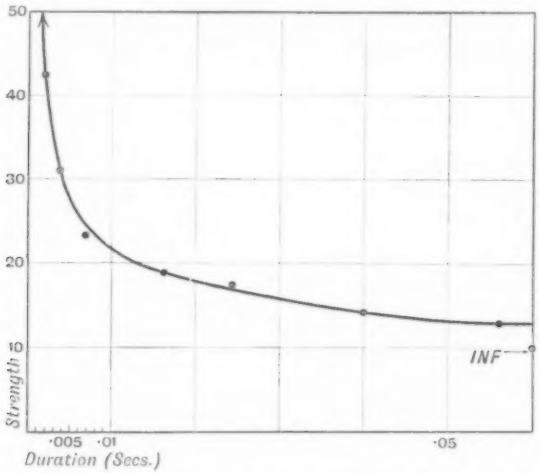

FIG. 5.—Tibialis anticus one and a half months after division of sciatic.

Case 3.—The leg was shot through in September, 1915, and the sciatic was exposed on October 11 and found to be divided. The ends were cleaned and sutured, and the curve was determined on November 3 and again on December 10. The chronaxie had the value 0·013 second at the first determination and 0·010 second at the second. For very strong currents the limiting durations are shorter than in Case 1, but otherwise the agreement is very close. The curve for November 3 is shown in fig. 5.

Case 4.—The patient was shot through the lumbo-sacral plexus on the right side in May, 1915, and had all the signs of complete division of the sciatic

He was examined once at the beginning of September and again a month later. The chronaxie was 0·010 second at the first determination and 0·0095 second at the second. There were no signs of recovery when the patient was discharged, but the condition of the nerve was never verified by operation.

Case 5.—The patient's fibula was fractured at its head by a bullet in June, 1915, and there was at once complete paralysis of the muscles supplied by the external popliteal. There was no recovery when he was examined on November 4. The chronaxie in this case was 0·013 second, and the curve agrees closely with those in figs. 4 and 5.

The different values of the chronaxie in these cases are collected in Table II, and it will be seen that they give a mean value of 0·011 second with extremes of 0·013 second and 0·0095 second.

From one point of view these results are only what might have been expected. The muscles had lost their response to faradic currents and retained that to galvanic currents, and therefore it is not surprising that the least duration of current which is necessary to excite them is very much longer than it is in a muscle with intact nerve supply. The form of the curve remains essentially the same though the time constant is altered, and this again is not to be wondered at in view of the fact that the same form of curve has been found for every excitable tissue which has been investigated hitherto.

From another point of view the results are certainly unexpected. In all, nine curves were determined in five different subjects at intervals varying from six weeks to nine months after the division of the nerve. In all these determinations the chronaxie was never greater than 0·013 second and never less than 0·0095 second. It is true that in every case the leg had been treated with daily massage, passive movements and galvanism very soon after the injury had occurred; but even so, it is surprising to find that the nature of the current required to excite varies so little with the lapse of time. As a matter of fact, the temporary condition of the muscle at the moment when it is examined does not affect the curve in the least. This is shown by some observations which were made on Case 1 to test the immediate effect of massage and exercise. The right tibialis anticus was examined at 9.30 a.m. before the leg was massaged, and the chronaxie was found to be 0·011 second. The leg was left motionless and exposed to cold air until 11.15 a.m. The curve was redetermined and was found to coincide with the first measurement. The leg was then massaged and exercised thoroughly for half an hour, and at 12.20 p.m. the curve was determined again. The chronaxie was still 0·011 second and the curve

had not altered in the least, although the contraction was certainly less sluggish than it had been before the massage. Clearly, then, the curve is not affected by such transitory conditions as the temperature and state of activity of the muscle at the moment when the determination is made, and some other cause must be looked for to explain the constancy of the results with different muscles. Either we must suppose that the excitability constants do not vary as the condition of the muscle passes from bad to worse, or else the condition of the muscle does not change appreciably within the time limits investigated.

The question is cleared up to some extent by the results given by muscles to which voluntary power is returning after an incomplete injury to the nerve. These are discussed in the following section.

TABLE II.—Tibialis Anticus after Complete Division of the Sciatic with no Signs of Recovery.

Case		Time after injury		Chronaxie
1	..	a, 6 months	.. .. ..	0·0095 second.
		b, 9 ,,	.. .. ..	0·011 ,,
2	..	a, 6 ,,	.. .. ..	0·011 ,,
		b, 6½ ,,	.. .. ..	0·011 ,,
3	..	a, 1½ ,,	.. .. ..	0·013 ,,
		b, 2½ ,,	.. .. ..	0·010 ,,
4	..	a, 4 ,,	.. .. ..	0·010 ,,
		b, 5 ,,	.. .. ..	0·0095 ,,
5	..	a, 5 ,,	(external popliteal) ..	0·013 ,,
			Mean value ..	0·011 ,,

In Cases 1, 2 and 3 the section of the nerve was verified by operation.

The Strength-duration Curve in Cases showing Evidence of Recovery.

The foregoing results show that in the healthy tibialis anticus with intact nerve supply the strength of current required to excite is doubled when the duration is reduced to 0·0003 second — 0·00008 second, whereas, if the nerve has degenerated, the duration at which the strength is doubled is about 0·011 second. Both cases give a curve of the same type, but the curve falls much more slowly in the latter case than in the former. To understand the significance of these curves it is clearly important to find out what happens when recovery is taking place, how the slow curve for denervated muscle becomes transformed into the rapid curve characteristic of muscle with intact nerve supply.

The ideal case to investigate would be one in which there had been a complete section of the nerve, with subsequent regeneration and commencing return of voluntary power. However, the sciatic takes many months to regenerate, and patients with complete sciatic division

are usually discharged long before there are any signs of recovery. The ulnar and median divided near the wrist recover much more rapidly, but the small muscles of the hand are very difficult to investigate by the present method on account of the spread of the current to neighbouring healthy muscles. Consequently the cases in the present section are limited to two of acute anterior poliomyelitis, one of toxic polyneuritis of unknown origin and one of incomplete injury to the sciatic by bullet wound. In all these cases the tibialis anticus had been completely paralysed, and at the time of investigation voluntary power had just returned in some degree to it or to neighbouring muscles.

The following is a short abstract of these cases :—

Case 6.—The patient, aged 19, had a typical attack of acute anterior poliomyelitis, beginning on September 5, 1915. When he was first examined there was moderate power in the arms, but very little in the trunk or legs. Power in the legs returned gradually during the months of November and December when he was under observation. The muscles were examined electrically on November 27, December 8, and December 26. During the whole of this time there was no response to faradism in the right tibialis anticus, and in the left there was a slight response to very strong currents. A slight degree of voluntary power was present on either side, but the left tibialis anticus was always stronger than the right and its power improved more rapidly. The determinations on November 27 and December 8 are shown in figs. 6 and 7. The curve for the right tibialis anticus is drawn as an unbroken line and that for the left is interrupted. All these curves show an obvious discontinuity and are composed of two simple curves of the same form but different constants. In fig. 6, for instance, in the curve for the right tibialis anticus there is a discontinuity when the duration is reduced to 0·0008 second and the strength has risen to 62. At this point the curve suddenly becomes horizontal and the strength remains constant at 62 until the duration has fallen to 0·0002 second. A further slight decrease in duration causes a sudden rise in the strength. In the curve for the left tibialis anticus the discontinuity occurs when the duration is 0·0024 second and the strength 35, and the curve does not begin to rise steeply again until the duration has fallen to 0·00024 second. In fig. 7 the discontinuities occur at longer durations and smaller current strengths. That for the right leg begins at a duration of 0·0017 second and a strength of 40, and that for the left at a duration of 0·0032 second and a strength of 29. The curves had not changed appreciably from this at the third determination on December 26.

Case 7.—This is the case of a patient, aged 28, who had an attack of acute poliomyelitis on October 8, 1915. The paralysis remained in the trunk, right arm and legs. He was examined on December 27, 1915. At this date the left tibialis anticus had moderate voluntary power, but did not react to faradism applied in the region of the motor point unless a very strong current was used.

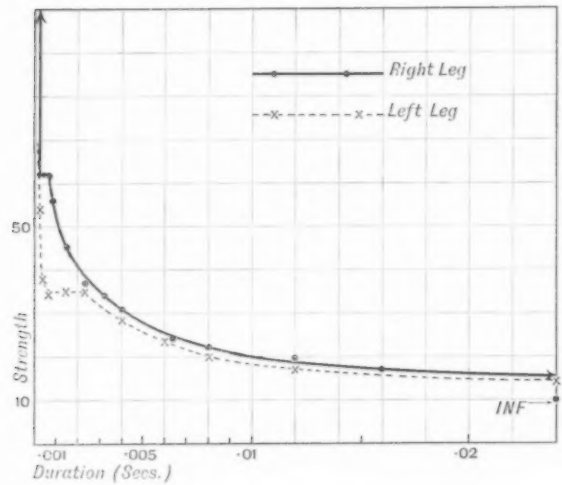

FIG. 6.—Tibialis anticus recovering from poliomyelitis.

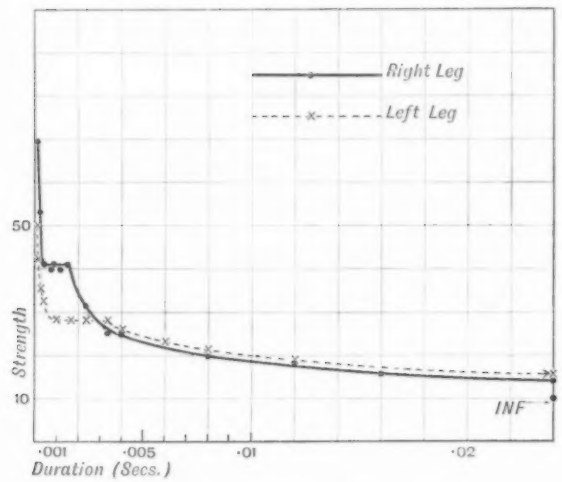

FIG. 7.—Same case as fig. 6, eleven days later.

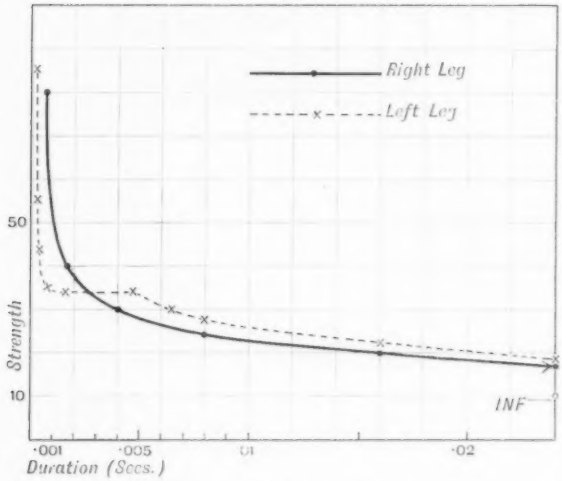

FIG. 8.—Poliomyelitis: slight return of power in left tibialis anticus, none in right.

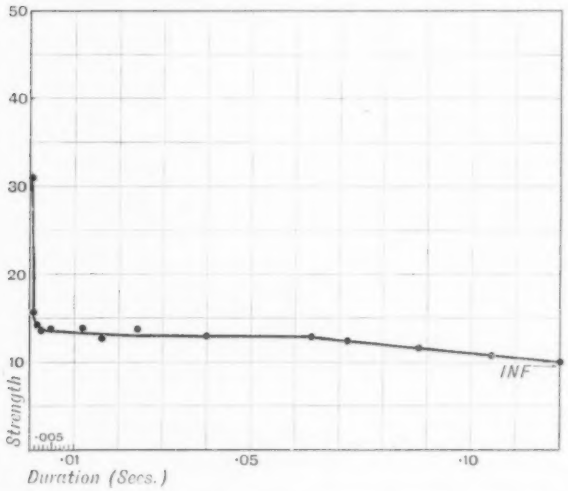

FIG. 9.—Same case as fig. 8: left tibialis anticus stimulated nearer the tendon.

It reacted more readily when the current was applied lower down the leg. The right tibialis anticus had no voluntary power at all and did not react to the strongest faradic currents which could be used. Fig. 8 shows the curves for both legs with the kathode applied high up near the motor point. That for the left tibialis anticus is drawn as an interrupted, and that for the right as an unbroken line. The right is a continuous curve, but the left shows a discontinuity when the strength is increased to 34 and the duration reduced to 0·0046 second. With smaller durations the strength remains constant and does not rise again until the duration is in the neighbourhood of 0·0004 second. Fig. 9 shows the curve for the left tibialis anticus with the electrode at a lower level. The curve rises gradually until the duration is reduced to 0·064 second and then remains constant at a strength of 14 until the duration is in the neighbourhood of 0·0004 second, after which it rises steeply.

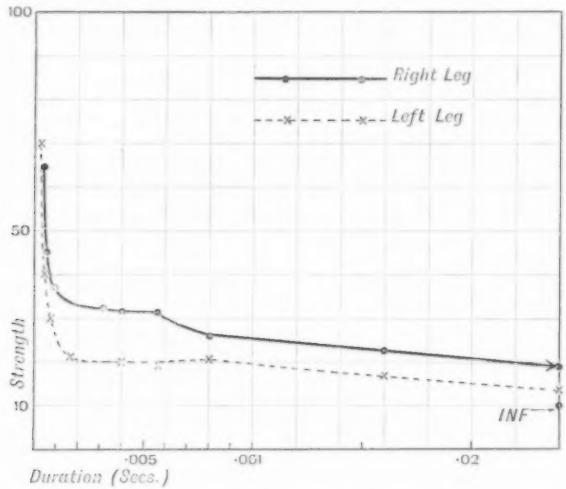

FIG. 10.—Toxic polyneuritis, recovering.

Case 8.—The patient had an attack of toxic polyneuritis of unknown origin in August, 1915. To begin with, both arms and legs were paralysed, but when he was examined he was recovering rapidly, had fair voluntary power in the arms and could walk for a short distance unaided. In spite of this the leg muscles showed no response to strong faradic currents and gave the typical reaction of degeneration with galvanic currents. The curves for the tibialis anticus on either side are shown in fig. 10. The curve for the right leg is an unbroken line and that for the left is interrupted. Both show a discontinuity, that on the left occurring when the strength is 20 and that on the right when the strength is 31.

Case 9.—The patient was shot through the right thigh in May, 1915. Immediately after the injury the leg was completely paralysed below the knee and there was complete loss of sensation over the area supplied by the sciatic. There was some return of voluntary power in the calf muscles in September, but the tibialis anticus was still paralysed. Its reaction to faradism was not determined. The strength-duration curve was determined on September 24 and again on October 7. At the first determination the current strength was not increased above 20; below this strength the curve is continuous and the chronaxie is 0·004 second. Fig. 11 shows the curve on October 7. There is a discontinuity at a strength of 24 and a duration of 0·0024 second. The lower part of the curve agrees in all respects with that determined on September 24.

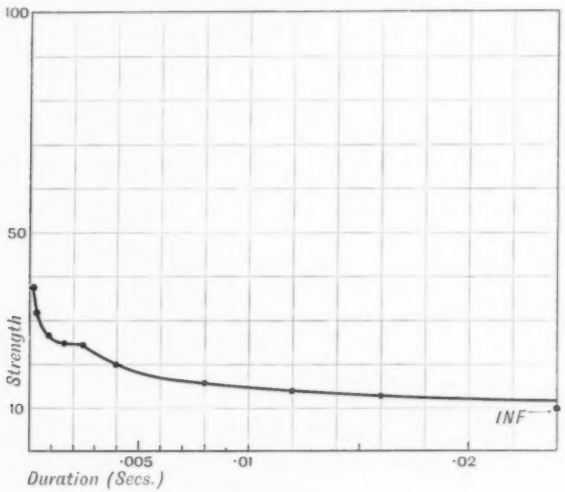

FIG. 11.—Incomplete sciatic injury, recovering.

A study of figs. 6 to 11 shows that there are certain common features in the strength-duration curves of all the muscles which gave evidence of recovery. In every case the curve is discontinuous and appears to be composed of two curves of the same form but with very different time-constants. The lower curve rises gradually at long durations; the upper starts from a higher base-line and does not begin to rise until the duration is very short. The point of intersection of the two curves varies widely, but it would appear from figs. 6 and 7 that it occurs at weaker strengths and longer durations as the condition of the paralysed muscle improves. If the time constants of these curves are

determined, it is clear that the upper curve has a short chronaxie which approximates closely with that for healthy muscle with intact nerve supply. In fact, the only point of difference between the curve for healthy muscle and the upper portion of these complex curves lies in the greater current strength needed in the case of the incompletely recovered muscle. Again, the lower half of the complex curve is very much like the curves for completely denervated muscle. The chronaxie of this part of the curve is certainly much more variable than the

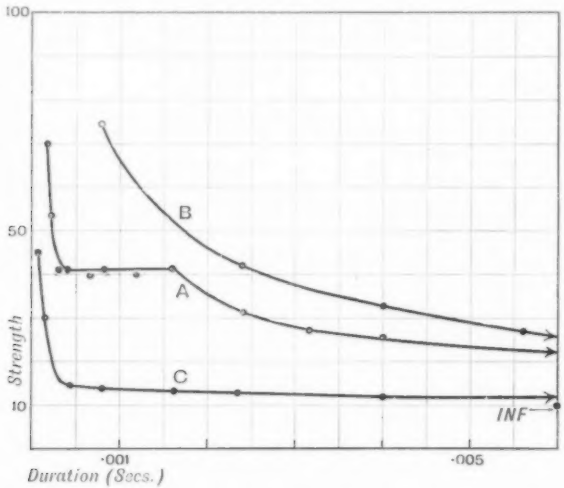

FIG. 12.—**A**, tibialis anticus recovering after poliomyelitis; **B**, tibialis anticus after complete degeneration of the sciatic; **C**, tibialis anticus with intact nerve supply.

chronaxie after division of the sciatic, but the figures are of the same order in both cases. A good example of this agreement is shown in fig. 12. In this figure the curve marked **A** is that for the right tibialis anticus in Case 6 (fig. 7 on a larger scale), **B** is a typical curve for denervated muscle (Case 1, fig. 4), and **C** is a curve for muscle with intact nerve supply. If the curve **C** could be made to rise from a higher base-line it is easy to see how the complex curve might be produced by a combination of the curve for intact with that for denervated muscle. There is certainly no sign of any gradual transformation of the curve for denervated muscle into that for healthy muscle, and this holds good for every case investigated.

The time constants of all the double curves are shown in Table III. The chronaxie of the slower curve is determined in the usual way—i.e., it is the duration corresponding to a strength 20, twice that at infinite duration. To determine the chronaxie of the more rapid part of the curve, the strength required when the discontinuity appears is supposed to be the strength at infinite duration. This amounts to the assumption that the rapid curve, if it could be investigated at long durations, would not fall appreciably below the value corresponding to the horizontal part of the curve. On this assumption the chronaxie is the least current duration required when the strength is twice that corresponding to the horizontal part of the curve. In some cases this must be found by extrapolation, as the actual strengths of current were not great enough.

The table brings out very clearly the agreement between the rapid part of the complex curve and the curve for muscle with intact nerve supply. The slower part of the curve agrees more or less with that for completely denervated muscle, but the close agreement of the average values is to some extent fallacious, since the extremes show a much wider variation in the case of incompletely recovered muscle than they do in denervated muscle.

TABLE III.—Commencing Recovery after Paralysis.

Case			Chronaxie of lower curve	Chronaxie of upper curve
6.	November 27 ..	Right ..	0·012 second ..	0·00008 second.
		Left ..	0·008 ,, ..	0·00014 ,,
	December 8 ..	Right ..	0·008 ,, ..	0·00016 ,,
		Left ..	0·010 ,, ..	0·00012 ,,
	December 26 ..	Right ..	— ,, ..	—
		Left ..	0·0095 ,, ..	0·00016 ,,
7.	— ..	Right ..	0·016 ,, ..	—
		Left ..	(*a*) 0·020 ,, ..	0·00010 ,,
			(*b*) 0·020 (?) ,, ..	0·00012 ,,
8.	— ..	Right ..	0·020 ,, ..	0·00024 ,,
		Left ..	0·0095 ,, ..	0·00040 ,,
9.	September 24 ..	— ..	0·004 ,, ..	—
	October 7 ..	— ..	0·004 ,, ..	0·00012 ,,

Extreme values {0·020 / 0·004} Mean 0·012 second. Extreme values {0·0004 / 0·00008} Mean 0·00016 second.

For denervated muscle (Table II) the corresponding values are:—

Extremes {0·013 / 0·0095} Mean 0·011 second.

For muscle with intact nerve supply (Table I) the values are:—

Extremes {0·00025 / 0·00008} Mean 0·00016 second.

Interpretation of Results.

We have seen that in muscle with intact nerve supply and in denervated muscle the strength-duration curve is of a constant form, but that the time-constant is much greater in the case of denervated muscle than it is in intact muscle. Further, the results obtained on muscles which are recovering from incomplete nerve lesions make it clear that the slow curve characteristic of denervated muscle does not return gradually and without any discontinuity until it approximates to that for intact muscle. Instead of this, the curve for recovering muscle is complex and is always made up of two distinct curves, of which the slower corresponds more or less with that for denervated muscle and the more rapid with that for intact muscle. In the earlier stages of recovery the more rapid curve does not appear until the current strength is several times the minimal value. As recovery progresses the rapid curve becomes evident with weaker and weaker current strengths, until eventually it would seem to oust the slower curve altogether.

This result is of very great importance, for it shows that during recovery the current takes effect upon two distinct excitable mechanisms with very different time constants. At first sight it might seem possible to explain this on the assumption that the current affected two groups of muscle-fibres in different states of recovery. In poliomyelitis the different fibres of a paralysed muscle do not always recover at the same rate, and a part of the muscle may have voluntary power and response to faradism while the rest is completely paralysed and responds to galvanism only. These fibres might be so intimately mixed that it would be impossible to distinguish one set from the other by mere palpation. Consequently the strength-duration curve might be composite because it was made up of curves for several sets of muscle-fibres in different stages of recovery. However, if this were the case we should expect to find not one discontinuity in the curve but several. In fact, there would be as many discontinuities as there were different stages of recovery in the fibres under investigation. Moreover, there would certainly be curves in which the time-constant had a value intermediate between that for denervated muscle and that for muscle with intact nerve supply. Neither of these possibilities is realized in figs. 6 to 11. The only other possible explanation is that the mechanism upon which the current takes effect in muscle with intact nerve supply is quite distinct from that in denervated muscle, and that the great

difference in the time-factor in the two cases is not due simply to an alteration in the conditions of one and the same mechanism. On this hypothesis the recovery of the muscle is shown by the appearance of the mechanism characteristic of normal muscle in addition to the mechanism characteristic of denervated muscle. In the earlier stages of recovery the former mechanism needs a much stronger current to excite it than does the latter, but as recovery progresses the rapid mechanism becomes more and more excitable, until eventually it replaces the slower mechanism altogether.

It is not difficult to find a satisfactory explanation of the nature of these two mechanisms. In the frog, Lucas and Lapicque have shown that the nerve-fibres in the trunk of the sciatic and the nerve-fibres in the substance of the sartorius and gastrocnemius react to much more rapid currents than do the muscle-fibres excited directly. Now the great difference between normal muscle and denervated muscle lies in the fact that the former possesses healthy nerve-fibres running in the substance of the muscle, whereas the latter does not. Evidently in normal muscles there are two distinct excitable mechanisms, the nerve-fibre and the muscle-fibre, whereas in denervated muscle there is one mechanism alone. From the results obtained on the frog we should expect that the nerve-fibres would have a much shorter chronaxie than the muscle-fibres, and hence it is easy to see why the intact muscle gives a much shorter chronaxie than the denervated muscle.

During recovery from injury to the nerve, traumatic or toxic, the intramuscular nerve-fibres become active again, but at first we may suppose they are less excitable than usual. Under these circumstances we should expect to find a double curve, weak currents of long duration affecting the muscle-fibres directly, and strong currents of short duration affecting the intramuscular nerve-fibres. A process of this kind has been demonstrated experimentally in the frog's sartorius by Keith Lucas. The strength-duration curve of this muscle may be either a rapid curve characteristic of the nerve-fibres, or a slower curve characteristic of muscle, or else a double curve showing both components. The type of curve in any particular case depends on the relative excitability of the nerve- and muscle-fibres and on the distribution of the nerve-fibres in the neighbourhood of the electrodes. When the muscle is treated with curare the nerve-fibres gradually cease to transmit impulses to the muscles, and consequently the more rapid component of the curve disappears, to return again when the effect of the curare works off. Fig. 13 shows a double curve obtained by Lucas [8] from the

sartorius of the frog, and the resemblance between this and the curves for human muscle in figs. 6 to 11 is self-evident. So far, then, the explanation is simple enough. However, there are one or two points which call for further discussion. In the first place, the mechanism which has been excited by currents of short duration has been identified with the intramuscular nerve-fibre. If this is so, we should expect to obtain a curve with the same constants when the current is applied to the nerve-trunk instead of to the muscle itself. The average value of the chronaxie when the kathode is applied to the external popliteal

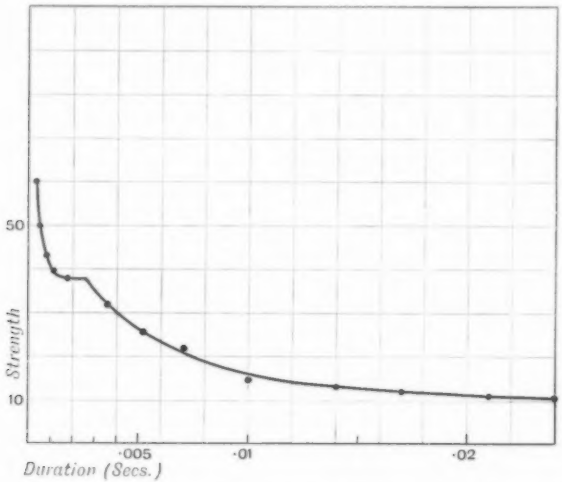

FIG. 13.—Frog's sartorius, showing stimulation of muscle-fibres (lower curve) and of intramuscular nerve-fibres (upper curve). (Keith Lucas).

worked out at 0·00025 second for four different cases. This is slightly longer than the value for the tibialis anticus. The difference may, of course, be due to experimental error.[1] However, there is another possible explanation which deserves mention. In the frog's muscle, in addition to the muscle- and nerve-fibres, Lucas has shown that there is a third excitable substance, which appears to correspond in distribution with the nerve-endings in the muscle. This substance has a shorter time-constant than the muscle-fibre, the chronaxie being 0·00017 second as

[1] Laugier (*loc. cit.*) finds that his *indice de vitesse* is the same for the nerve-trunk and for the muscle with intact nerve supply, see p. [31].

against 0·0005 second for the nerve. In the case of human muscles it is conceivable that a current applied to the muscle may excite a mechanism in the nerve-endings rather than in the intramuscular nerve, and this may explain the slower value of the chronaxie for the nerve-trunk. However, in the absence of more reliable figures, this cannot be insisted upon.

There is another possibility which must be discussed shortly. It is sometimes held that voluntary muscle is made up of two components—a fibrillar substance which reacts rapidly and a sarcoplasmic substance which reacts slowly. These two substances might, perhaps, be identified with the two excitable substances in human muscle, the fibrillar substance disappearing when the nerve degenerates. However, the idea has little or nothing in its favour. The independent existence of the fibrillar and the sarcoplasmic substances in mammalian muscle has never been proved, and there is nothing to show that they have the distinct properties with which they are credited. Furthermore, the electric reactions of the cold-blooded tissues are certainly due to the effect of the current on muscle-fibres and nerve-fibres, and it is difficult to believe that the reactions in human muscle are due to an entirely different mechanism. Much the same objection may be brought against the view that the two excitable mechanisms are to be identified with the white and red fibres of the muscle. It is true that the existence of these two sets of fibres is not in doubt, and it is true also that the white fibres degenerate more rapidly than the red. Again, the white fibres give a brisker contraction when they are stimulated, and therefore they might well react to currents of shorter duration. In human muscle the two types of fibre are intimately mixed, and so we might expect to find evidence of two different constants in the strength-duration curve. However, we have seen that the chronaxie of the rapid component of the double curve is equal to or slightly shorter than that of the nerve-trunk itself. This in itself is very much against the suggestion that the rapid curve is due to the white muscle-fibres rather than the nerve-fibres or nerve-endings; for, setting aside the comparatively close agreement between the chronaxie of the rapid curve and that of the nerve, no other case is known in which a muscle-fibre has a time constant equal to or shorter than that of the nerve-fibre which supplies it. Moreover, if the short chronaxie were due to the white muscle-fibres, we should not expect it to disappear until the muscle showed definite signs of wasting or to reappear until the wasting began to improve. Consequently, we must revert to the idea that

the two mechanisms in question are the muscle-fibre and the nerve-fibre.

A further point of interest concerns the value of the chronaxie for denervated muscle. After complete section of the sciatic the chronaxie always lay between 0·013 second and 0·009 second, and it has been suggested that this value is characteristic of muscle-fibre excited directly. It is naturally impossible to verify this by direct experiment on a human subject, as the effect of the nerve-fibres would have to be eliminated by curare or some such means. In the frog the chronaxie for muscle-fibre is about 0·007 second at 15° C., although we might naturally expect it to be longer than that for the muscles of a warm-blooded animal. This suggests the possibility that the chronaxie for human muscle-fibre would be really shorter than 0·01 second if it could be measured when the fibre was in a healthy condition, and that after the nerve is destroyed the chronaxie becomes longer on account of the abnormal state of the muscle. This view is upheld by the fact that in Case 9, where the nerve injury was incomplete, the chronaxie of the slower component of the curve was 0·004 second, a value which is less than half the average for denervated muscle. In spite of this it seems, on the whole, more probable that the figure of 0·01 second is the average value for muscle-fibres, and that the short value in Case 9 is due to an individual peculiarity and not to the improved condition of the muscle. If this were not the case we should expect the chronaxie to become longer and longer with the lapse of time following section of the nerve. The figures in Table II show that this lengthening does not occur. Again, in Case 7 (poliomyelitis) the chronaxie of the lower part of the curve is 0·02 second, although there was some return of voluntary power in the muscle, and although the chronaxie for the other tibialis anticus, which did not show any sign of recovery, was only 0·016 second. Consequently, the restitution of functionally active nerve-fibres is certainly not followed by an immediate shortening of the chronaxie for muscle-fibres. This does not imply that the chronaxie for muscle does not become longer as the muscle wastes and becomes converted into fibrous tissue. The muscles examined in Table II had all been treated by massage and electricity, and they showed very little wasting; on the other hand, in a few cases of ulnar and median injuries, with marked wasting of the small muscles of the hand, the chronaxie appeared to be considerably longer, 0·025 second or 0·03 second at least. These results are only rough approximations, as the method is very uncertain when applied to small denervated muscles in close contact

with small healthy muscles. Still, no doubt the chronaxie of human muscle-fibre may vary from 0·004 second to 0·03 second, or longer according to the state of the tissue. The important fact remains that functional connexion with the central nervous system may be restored, although the chronaxie of the muscle-fibres is twice as long as the average value for denervated muscle. The precise bearing of this result will be seen in the following section.

The conclusions arrived at in the present section may be stated briefly as follows: In muscle with intact nerve supply there are two distinct mechanisms upon which an electric current may take effect. These mechanisms are: (*a*) the intramuscular nerve-fibres, and (*b*) the muscle-fibres themselves. The nerve-fibre responds to currents of much shorter duration than the muscle-fibre, and in healthy muscle the strength-duration curve is always continuous and characteristic of nerve-fibre alone. In muscle which is in process of recovery after a nerve lesion the curve is discontinuous and is made up of two simple curves, one with the short time constant characteristic of nerve and the other with the long time constant characteristic of muscle. After complete degeneration of the nerve the curve is continuous and has the long time-constant characteristic of muscle. The constant may vary with the condition of the muscle, but its precise value does not affect the possibility of reunion with the nerve.

The Bearing of these Results on Diagnosis and Prognosis.

If we accept the foregoing interpretation of the changes which follow injuries to the nerve we can draw certain conclusions regarding the possibility of electrical testing in general without reference to any particular method. For instance, it is clear that after a lesion which has produced complete degeneration of the nerve-fibres the electric reactions of the muscle itself can give no information at all as to the state of the nerve at the site of the injury. All we can hope to decide is whether the muscle is or is not in a fit state to recover its voluntary power when the nerve-fibres have regenerated. We cannot tell whether the lesion is one which makes regeneration impossible and therefore demands operation, or whether regenerated fibres are already growing down towards the muscle. The present observations show that the condition of the muscle itself, as indicated by the time constant, is of no great importance. It may remain for long periods unchanged after the complete degeneration of the nerve, and voluntary power may

return although the constant is twice as long as that six months after complete section (Case 7). The all-important factor is the condition of the nerve at the site of injury, and this we cannot hope to determine by electrical methods.

The position is altered when there are some nerve-fibres peripheral to the lesion which retain or have regained their excitability to electric currents. The presence of these fibres may be detected from the complex nature of the strength-duration curve and the production of a response in the muscle to currents of very short duration. If these fibres become more and more easily excitable it is safe to assume that the condition of the nerve is improving. In such cases the determination of the electric constants would show that the prognosis was favourable. However, these determinations would be of value only in those cases in which the possibility of recovery could not be deduced by simpler methods. For instance, if there is any return of voluntary power in the muscle there is clearly no need of an electrical examination to tell us that some of the nerve-fibres have regained their function. In three out of four of the cases of commencing recovery which were examined by the present method the return of a slight degree of voluntary power appeared to coincide with the reappearance of the curve with the short time-constant, and therefore with the reappearance of nerve-fibres which would respond to stimulation by electricity. In the fourth case (gunshot wound of the right thigh, Case 9) the strength-duration curve showed that some of the nerve-fibres could be excited electrically although there was no return of voluntary power in the tibialis anticus. Even so, the electric constants were not needed to show that the nerve was recovering, as there was already a considerable return of power in the calf muscles. Nevertheless, in so far as its history is concerned, the case is typical of a large number of incomplete nerve injuries caused by gunshot wounds, in which the paralysis clears up without operation, and much more rapidly than it should do if the nerve-fibres below the site of injury had degenerated completely. In these cases it is evident that the nerve-fibres below the injury must be still in some kind of trophic connexion with the motor cells in the cord, though they are unable to transmit impulses from the central nervous system to the muscle. Unfortunately, Case 9 was the only one of this class of injury which could be investigated by the present method, but it is not unreasonable to suppose that most if not all of them would agree with it in showing evidence of nerve-fibres peripheral to the lesion and yet capable of responding to electric stimuli. If so, the determination of the

strength-duration curve would give valuable evidence of the likelihood of recovery. When the curve does not show the characteristic discontinuity, we can only say that the nerve-fibres peripheral to the injury are inexcitable and that the possibility of recovery must remain in doubt. In such a case we may say with certainty that there is no method of electrical testing which will help to solve the question, since the current takes effect on the muscle-fibres alone, and the state of the muscle-fibres gives no indication of the state of the nerve.

In conclusion, we may say that a certain prognosis can be given only in those cases in which the nerve-fibres peripheral to the injury retain some measure of excitability. The presence of such fibres is shown by the complex type of strength-duration curve and the efficacy of currents of very short duration. How far their presence may be detected by the simpler methods of testing in vogue at present is a question which will be discussed in the following section.

The value of these results in diagnosis is another matter. To a certain extent any method of diagnosis which gives additional information as to the state of a diseased tissue must be counted of value, even though the information has no direct bearing on the treatment and prognosis of the case. The strength-duration curve gives definite information as to the state of the excitable mechanisms in nerve- and muscle-fibre, and this information may be expressed in a quantitative form. Furthermore Lapicque, Keith Lucas and A. V. Hill have put forward theories as to the nature of electric excitation in which the constants of the strength-duration curve are given definite physical interpretations. These theories are based on Nernst's [11] original hypothesis that, in order to excite, the current must bring about a certain concentration of ions at the surface of a semi-permeable membrane in a substance of the fibre. Thus in Hill's theory the constants of the curve enable us to tell the charge on the ions, their rate of diffusion, the distance separating the membranes at which they take effect and the degree of concentration which must be attained in a given time for excitation to take place. These may be calculated as readily in the case of human excitable tissues as in those of the frog, and in this way it should be possible to relate a change in the condition of the muscle to a change in the diffusibility of the effective ions or the degree of concentration which must be attained at the membranes, &c. No attempt has been made to treat the present results in this way, because they are too few for such an elaboration and because the present theories of excitation are admittedly incomplete and in need of

alteration. For the present it must suffice to point out the possibilities of exact diagnosis which might be made on these lines.

Present Methods of Electrical Testing.

We have seen that the most important function of electrical testing is to determine the presence or absence of excitable nerve-fibres peripheral to the damaged area. If these fibres are present some weeks after the injury, the prognosis is good, and recovery may take place without operation. If they are absent, the prognosis is uncertain, but there is evidently no need to delay operation. It follows that the different methods of electrical testing must be valued according to their ability to detect these fibres. When the complete strength-duration curve is determined, the presence of active fibres is shown by the complex type of curve and the response to currents of very short duration. A current of 0·0004 second will excite nerve-fibres if it is strong enough, but it will not excite muscle-fibres, however strong it may be. So if we could always use a current of this duration and of variable strength there would be no need to determine the full curve. It remains to be seen how far this may be done with the methods in use at present.

(1) *The faradic and galvanic current.*—At first sight it might appear that the ordinary method of testing with the induction coil would be accurate enough, since the faradic current is of such a duration that it will excite nerve- but not muscle-fibre. However, it is evidently not at all suited to detect the presence of nerve-fibres if these are relatively inexcitable. It is well known that a muscle may regain some degree of voluntary power long before it shows any response to faradism, and in such a muscle there must be some functionally active nerve-fibres. Such a condition was found in all the cases of incomplete recovery described in this paper. The explanation of this state of affairs may be seen from fig. 7. In this case both legs had some return of voluntary power and the left tibialis anticus reacted slightly to faradism, whereas the right did not react at all. The strength-duration curves show that active nerve-fibres are present in both muscles, but in the right leg the current must have a strength of 40 if it is to affect the nerve, whereas in the left it need not be stronger than 29. With a short duration it is quite possible to employ a constant current of strength 40 or more without causing much pain, because the whole of the current is effective in stimulating the tissue. However, a faradic current of equal stimulating effect would be far too painful, because the

useful part of the current is only that fraction of the discharge when the electromotive force is at or near its maximum, and the remainder adds to the pain without taking any effect on the excitable tissue. Consequently the right tibialis anticus was put down as inactive to faradism because it was inactive to faradic currents of a strength which could be borne by the patient without an anæsthetic. Presumably the same holds good for every case in which there is voluntary power but no response to faradism. The nerve-fibres need a strong current to excite them, and a faradic current of this strength cannot be tolerated because of the pain it would cause.

(2) *The condenser method.*—This is clearly superior to the induction coil method because it is possible to select the duration of the discharge as well as the strength. Indeed, with some elaboration it would be possible to map out the full strength-duration curve with a series of condensers of different capacities. The discharge is more painful than that of a constant current, because the electromotive force falls off rapidly and the latter half of the discharge is useless. The duration of the discharge depends on the total resistance in the circuit as well as on the capacity of the condenser, but for practical purposes the difference in the resistance of two similar limbs is not great enough to matter. Consequently, it should be quite possible to select a capacity which would affect nerve-fibres without affecting muscle and to use this for detecting the presence of active nerve-fibres in incomplete lesions. It would be necessary to have some means of varying the strength of the discharge, or else to use a discharge so strong that there would be no chance of missing relatively inexcitable nerve-fibres.

The ordinary method of using condensers gives information of very doubtful value. If the muscle will respond to discharges of very short duration—0·05 mf. or less—we may safely infer that the nerve contains active fibres; but if a longer discharge is necessary, its precise value tells us nothing unless we know also the strength of the discharge relative to the strength required when the duration is infinite. If we do not know this, we cannot fix even one point in the strength-duration curve, and a change in the least capacity required to excite might be due to nothing more important than a change in the general excitability of the tissue brought about by increased skin resistance or excess of fluid in the subcutaneous tissues.

Consequently, there is nothing to be gained by stating the fact that a muscle responds to the discharge of a condenser of, say, 1 mf. capacity, unless we can add that the strength required must be a

definite multiple of that required at infinite duration. Without this information it is clearly quite impossible to determine the constants of the tissue.

(3) *Laugier's* [5] *method.*—This amounts to an attempt to determine the constants of the strength-duration curve by means of two stimuli of different duration. These are furnished by the make and break shocks of an induction coil, since the durations of these shocks are fixed quantities depending on the dimensions of the coil, and the duration at make is several times as long as that at break. A comparison of the strengths of current required to excite at make and at break gives a quantity which Laugier calls the *indice de vitesse* of the tissue, and which is proportional to the slope of the strength-duration curve between the points corresponding to the durations of the make and break shocks. The index is not affected by simple changes in the excitability of the tissue, and a change in the index always denotes a change in the slope of the curve. The method is ingenious and simple to apply, but it is based on a misconception of the changes which take place when the nerve is damaged. If the rapid curve characteristic of normal muscle were transformed gradually and without discontinuity into the slow curve of denervated muscle, and vice versa, the slope of the curve between two fixed points should give all the information necessary to determine the condition of the tissue. However, we have seen that the transition is abrupt and that the two curves are quite distinct, the rapid curve becoming more and more prominent as the process of recovery advances. When the curve is discontinuous, the slope between two fixed points will depend on the position of these points in relation to the discontinuity, and although a change in the slope will imply a change in the complex curve, the notion of the *indice de vitesse* loses its simplicity and is no longer a quantity definitely related to the constants of the tissue under examination.

Practically the method has the disadvantage that it cannot be applied to a muscle which has lost its excitability to faradic currents, since the stimuli are necessarily of very short duration. In any case it cannot be said to take the place of the complete determination of the strength-duration curve, since the double curve cannot be defined by two points only, whatever may be the durations corresponding to these points.

SUMMARY.

The curve which expresses the relation between the least strength and the least duration of the current required to excite has the same form for human tissues as it has for the tissues of cold-blooded animals. The time-constant of the curve is determined by the duration at which the current strength must be twice the minimal value. This duration is characteristic of the tissue examined, and it has been named the "chronaxie." In healthy muscle with intact nerve supply the chronaxie is very short, 0·00016 second on the average, and it is slightly longer when the electrode is applied over the nerve-trunk instead of to the muscle directly. When the nerve has degenerated the chronaxie is very much longer. Its average value is 0·011 second, and, in the case of the tibialis anticus at any rate, it shows surprisingly little variation with increased lapse of time following the injury. When the muscle is in process of recovery, the slow curve of denervated muscle does not pass gradually into the rapid curve of healthy muscle; instead of this, the first sign of recovery is marked by the appearance of a discontinuity in the strength-duration curve. With very strong currents the curve has the short time-constant characteristic of healthy muscle, but with weaker strengths a slower curve appears, and this has the long time-constant of denervated muscle. The production of these double curves shows that there are two distinct mechanisms upon which the current may take effect; only the slower mechanism is present in denervated muscle, and as recovery takes place the more rapid mechanism comes into play and eventually predominates, to the exclusion of the slower mechanism. Reasons are given for the belief that these two mechanisms are to be identified with the muscle-fibre and the nerve-fibre or nerve-ending. Thus the appearance of the discontinuity in the strength-duration curve and the response to currents of very short duration shows that there are some excitable nerve-fibres peripheral to the injury. This is to be expected in those cases of incomplete injury where the trophic influence of the nerve cells is not abolished, although impulses cannot pass from the central nervous system to the muscle. When the curve is continuous and has the slow chronaxie only, all that can be said is that there are no excitable nerve-fibres peripheral to the injury. The possibility of regeneration depends on the state of the nerve at the site of injury, and this cannot be determined electrically. The condition of the muscle is not of very great importance, for voluntary power may begin to return although the chronaxie of the muscle-fibres is twice as long as it is nine months after complete

degeneration of the nerve. It follows that the most important function of electrical testing is to decide whether there are any excitable nerve-fibres peripheral to the injury. If there are, and if they are becoming more excitable, then there is no need to operate; if not, we cannot tell whether the nerve will regenerate or not, and there is no reason to delay operation.

The different methods of testing in vogue at present give some information as to the presence or absence of these fibres. The method of condenser discharges is the most reliable, but the usual method needs several modifications; in particular, the strength of current must be a definite multiple of that required at infinite duration, otherwise a change in the general resistance of the limb, &c., may be mistaken for a change in the time constant of the muscle.

The present investigations were carried out on the military cases at the National Hospital for the Paralysed and Epileptic, Queen Square, and I am deeply indebted to the medical and surgical staff of the Hospital for allowing me to make use of these results.

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DISTURBANCES OF VISION FROM CEREBRAL LESIONS, WITH SPECIAL REFERENCE TO THE CORTICAL REPRESENTATION OF THE MACULA.[1]

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AND

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In our work in the base hospitals in France during the past eighteen months we have observed a very large number of cases in which vision was affected by the lesions of various portions of the optic system, but time and opportunity have not permitted a careful and complete examination of all. Consequently, in many cases of considerable clinical importance we possess only scanty and incomplete notes; but by selecting for thorough investigation a certain number of suitable cases we have been able to collect a group of facts that have an important bearing on the cerebral localization of vision, and more particularly on the representation of different regions of the retina in the cortex.

Owing to the conditions under which we have worked, most of our observations were necessarily made at a relatively early date after the infliction of the wound; we recognize that this fact makes possible the objection that, as our cases were mainly examined during the stage in which the effects of shock or diaschisis were still present, the visual defects we describe may have been due to functional disturbances rather than to localized injuries of the corresponding cortical areas or of their centripetal fibres: but if we can show that there is a constant relation between the probable site of the injury and the form of the visual defect, it is obvious that certain general conclusions at least will be justifiable.

The fact that most of our patients were investigated in the early stages also presented certain technical difficulties; as most were confined to bed a small hand perimeter had to be employed, but in some the observations were later controlled by a McHardy perimeter. We have

[1] Read before the Ophthalmological Section of the Royal Society of Medicine, March 22, 1916.

also employed a modification of Bjerrum's screen[1] to determine the exact relations of smaller defects. Further, as such patients tire easily and quickly, repeated examinations were often necessary. On the other hand, the fact that most of the wounds were recent has enabled us to make many interesting observations on the mode and rate of recovery of vision from different forms of injury.

Since the time of Munk, who from his experimental observations attempted to project the retina directly on to the cerebral cortex, the localization of visual function has excited much interest, but until relatively recently nothing was known of the exact limits of the visual area, or of the regional representation of the retina within it. Certain authors, and especially Henschen and J. S. Bolton, have, however, discovered pathological evidence that the visual area coincides with that cortical zone of special structure which is now generally known as the area striata (fig. 1). This is the area, distinguished by Gennari's line, which lies within and on both lips of the calcarine fissure and which, even in the higher races of mankind, but to a greater extent in the lower, extends to and around the pole of the occipital lobe. There is now considerable evidence, due chiefly to the work of Henschen, that the upper half of each retina is represented in the upper parts of these areas, and the lower in the lower walls and lips of the calcarine fissures; destruction of the upper portion of the area striata on one side would consequently produce a lower quadrantic homonymous hemianopia in the opposite halves of the visual fields, and vice versa.

On the other hand, nothing is definitely known on the correspondence between various concentric zones of the retina and the different segments of the area striata.

The question of the cortical representation of the macula has for a

[1] A description of this modification may be useful, especially to those engaged in similar work. A large sheet of paper (double foolscap), covered with black cloth, is placed on a flat board and both are pinned to it. A small drawing-pin serves as a fixation point. The test object is carried on the blunt end of a steel pin, about ½ cm. in length, which is fixed transversely across the end of a dark metal rod, so that its point projects about 1 mm. on the opposite side. The test object thus fixed on the end of the rod is moved slowly from the blind region along the screen until the patient sees it; then the carrier is simply pressed against the board so that the point of the pin penetrates the cloth and marks the paper beneath it.

A large number of observations are taken. If the distance of the fixation point from the eye is known—we generally use it at a distance of 1 m.—the record thus obtained can be transferred to an ordinary or to a special perimeter chart.

One advantage of this method is that as there are no lines or marks on the screen which can influence the patient or the observer, the records obtained by it are absolutely unbiassed.

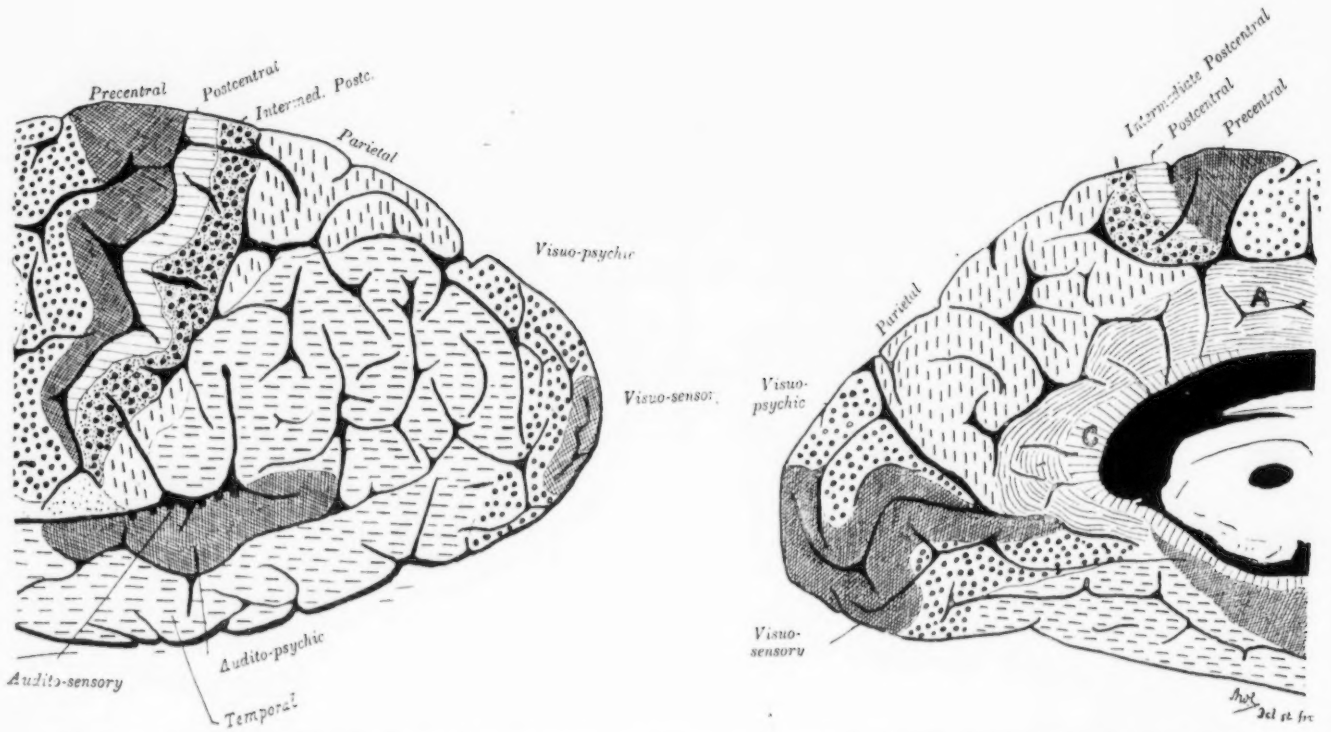

FIG. 1.—To show the superficial distribution of the area striata (visuo-sensory) on the mesial and lateral surfaces of the hemisphere (*Campbell*).

long time excited much interest. Owing to the fact that in the majority of those cases of homonymous hemianopia due to vascular lesions which are seen in civil practice, vision is unaffected for a distance of 2° to 10° to the blind side of the fixation point, it was for a time generally assumed that each macular area is represented in both hemispheres; this hypothesis was apparently supported by the anatomical observation that at the chiasma branches of the macular fibres from each eye pass into each optic tract. But the fact that in bilateral hemianopias due to lesions of both occipital lobes central vision often persists confuted this view, and gave origin to the hypothesis that the macular centre must lie outside the area striata, or may not indeed be locally represented in any part of the cortex (von Monakow).

Others have attempted to explain the macular escape in hemianopia by assuming that the two cortical macular centres are connected by callosal commissural fibres (Lenz, Heine), or by the hypothesis that the physiologically more highly developed macular impulses pass more easily through an incomplete block (Ronne).

Within recent years, however, many attempts have been made to determine a localized macular centre in the cortex. Henschen, for instance, first assumed that the macular focus lies in the anterior portion of the calcarine cortex, and later that it extends along the whole floor of the calcarine fissure. J. S. Bolton, too, has recently assumed that the "calcarine core" of the visual cortex is the anatomical basis for macular vision. On the other hand, Inouye, in his excellent monograph on the visual disturbances observed after gunshot injuries of the occipital lobes inflicted in the Russo-Japanese War, brings evidence showing that the macular centre must lie towards the pole of the occipital lobe; while Lenz, in a general review, concludes that though certain published cases indicate its localization anteriorly in the calcarine cortex, more are in favour of its representation posteriorly in this region.

Our own observations will bear on all these points. It must be recognized, however, that there are difficulties in determining the exact site of the essential lesion in the optic system, and even when the position of the injury is exactly known, it is not always easy to correlate the visual disturbance with it. This is largely due to the fact that, as the optic radiations in sweeping backwards along the outer side of, and especially behind, the posterior horn of the ventricle, lie in relatively close relation to the area striata, either these or the cortex, or both, may be affected by the one lesion, and consequently the exact cause of the visual disturbance may be uncertain. Since,

however, the fibres of the radiations that reach the most posterior part of the pole are probably distributed only to the most posterior part of the calcarine cortex, visual defects associated with their injury here may bear directly on the question of cortical localization. On the other hand, an extensive lesion in the middle or anterior portion of the calcarine cortex may involve any or all of the fibres of the radiations, and the associated visual defects may give us no clue to localization.

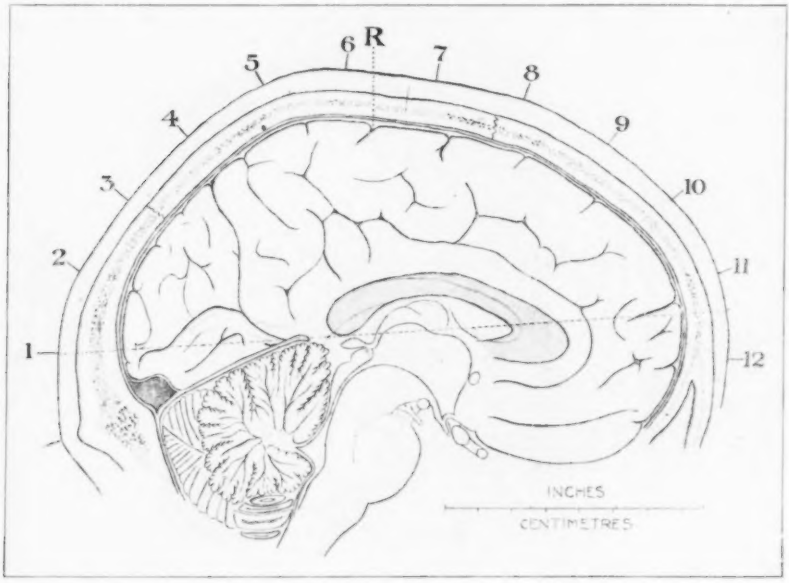

FIG. 2.—Mesial sagittal section of an average-sized head (distance between nasion and inion 13½ in., or 34 cm.) to show the relation of the calcarine fissure to the inion. The lines vertical to the surface of the figure indicate the distance of each point from the inion in inches, measured along the scalp in the middle line of the head.

There is, however, considerable evidence to show that the fibres in the radiations are to some extent arranged according to their destination in the area striata. Otherwise many published records would be unintelligible.

The injuries in our cases include penetrating and perforating wounds of the cranium by rifle bullets, shell fragments and shrapnel, as well as local concussions and depressed fractures.

The portions of the brain injured can be approximately determined when there is a depressed fracture or a penetrating wound of the skull by noting its relation to certain fixed points, as the inion, supplemented by a stereoscopic X-ray examination. If the relations of the calcarine fissure and of the area striata to this fixed point are approximately

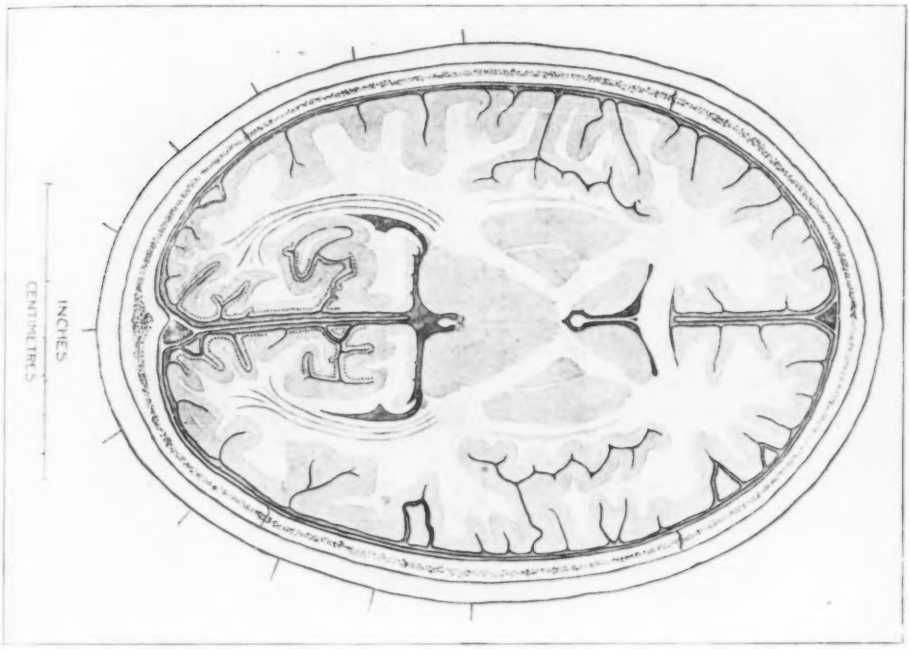

FIG. 3.—A horizontal section through an average-sized head, taken 1 in. above the tip of the inion and 2 in. above the nasion, in the plane represented by the broken line in fig. 2, to show the relations of the area striata. This is indicated by a broken line in the occipital cortex. The marks on the surface of the scalp represent inches measured in this plane from the middle line posteriorly.

constant, as we have found them to be (fig. 2), the position of the cerebral injury can be often fixed within relatively close limits, and if the anatomical relations of the whole of the visual cortex, as seen in both sagittal and horizontal sections (fig. 3), are also known, then in the case of traversing bullets and fragments of shell, the entrance and exit wounds of which can be measured from a fixed point, the track of the missile can be calculated, since experience has shown

that bullets usually take a straight course between the entrance and exit wounds. It must be remembered, however, that the amount of destruction produced by such missiles may vary much. In many of the cases we have been also able to determine the approximate site and extent of the cerebral injury during operation, and in a few cases we have been able also to verify it by *post-mortem* examination. But though the exact localization of the lesion may appear to be indefinite, the consensus of evidence will be, we believe, sufficiently strong to justify certain positive conclusions.

Quadrantic Defect in the Visual Fields.

We have been able to observe a certain number of cases of so-called quadrantic hemianopia, and will first deal with them, selecting those that throw most light on the question of the cortical representation of the upper or of the lower quadrants of the retina:—

Case 1.—Lieutenant C. was wounded February 26, 1915, by a fragment of shell. He was unconscious for a short time, and afterwards had much headache, and found his sight was affected. He was operated upon next day in a casualty clearing station, when pieces of depressed bone were removed, and was sent to the base a week later.

Wound.—There was then an oval open wound surrounded by a flap incision; its centre was $3\frac{1}{2}$ in. (9 cm.) above and 1 in. (2·5 cm.) to the right of the inion, and from here a track, closed at its lower end, but open for about $\frac{3}{4}$ in. (2 cm.), passed horizontally forwards into the brain. He had then loss of vision in the lower left quadrants which came to within 5° of the fixation point. He presented no other abnormal symptoms (fig. 4). His wound healed rapidly, and he was evacuated to England.

It is obvious that in this case the wound, which was of considerable size, lay above the right calcarine fissure.

Case 2.—Staff-Serjeant M., 20,175, was wounded by a piece of shell-casing on May 23, 1915. He was unconscious for a short time, and later had very severe headache and vomiting. He also found his vision seriously affected at first. When he arrived at the base next day there was a large wound, the centre of which lay $2\frac{1}{2}$ in. (6·5 cm.) above the inion and $\frac{1}{4}$ in. (0·5 cm.) to the right of the middle line. An X-ray plate showed fragments of bone and a small piece of metal driven into the brain, directly forwards, to a considerable depth; these were removed with some septic and disintegrated brain, and the track drained. He made an uninterrupted recovery and was transferred to England about three weeks later. While under observation he had a complete loss of vision in the lower left quadrants and slight limitation in the periphery of the left upper quadrants (fig. 5).

In this case; too, in which a considerable amount of brain was probably damaged, the lesion lay above the level of the right calcarine fissure.

Case 3.—Lance-Corporal M., 4,940, was wounded by a bullet on March 24, 1915. He was not unconscious, but had severe frontal headache and vomiting for some days. He was completely blind at first, but on the fifth day was able to recognize light to the right of the fixation point.

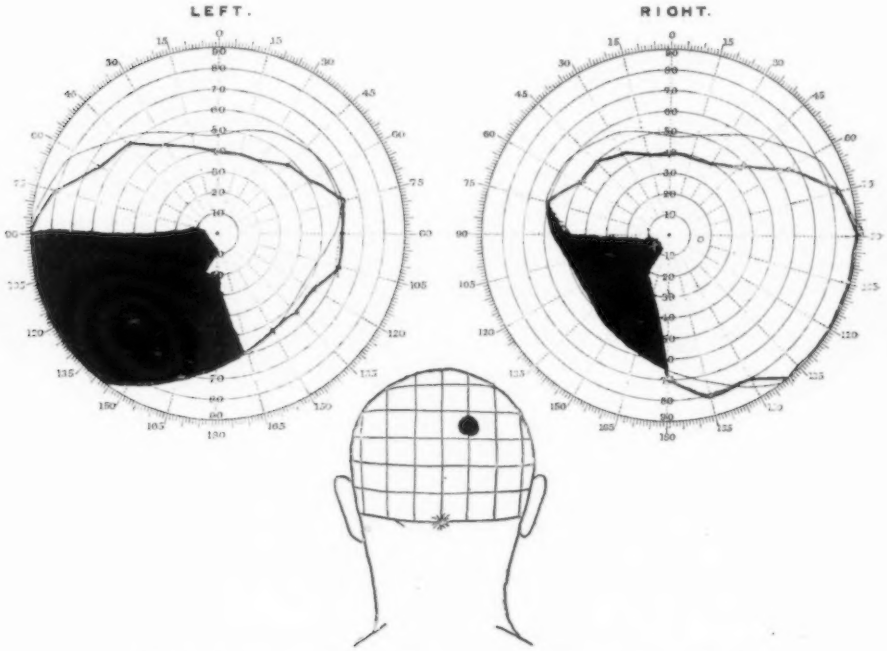

FIG. 4.—In this and the following figures the position of the wound is represented approximately on a diagram of the back of the head. The horizontal lines on this represent the distance in inches of the plane in inches above the inion, the vertical the distance in inches from the middle line of the skull.

The *wound*, which was 1½ in. (4 cm.) above the inion, extended across the middle line; it had been operated upon in a casualty clearing station, and depressed fragments of bone were removed. An X-ray examination later showed a defect in the skull, chiefly to the right, and a linear fracture running forwards to the right side. When seen at the base five days later he had distinct vision only immediately to the right of the fixation point, but on the seventh day had an almost full field in the right upper quadrant, but could recognize colours only by central vision. On the fifteenth day after the infliction of the wound there

was some further recovery in the lower right quadrant near the fixation point, and the colour fields in the seeing portion of the fields was almost full (fig. 6); on the left the blindness extended up to the fixation point.

In this case the lesion lay immediately above the posterior end of the calcarine fissures; it evidently produced considerable destruction in the right hemisphere, and probably affected only the upper portion of the calcarine cortex on the left.

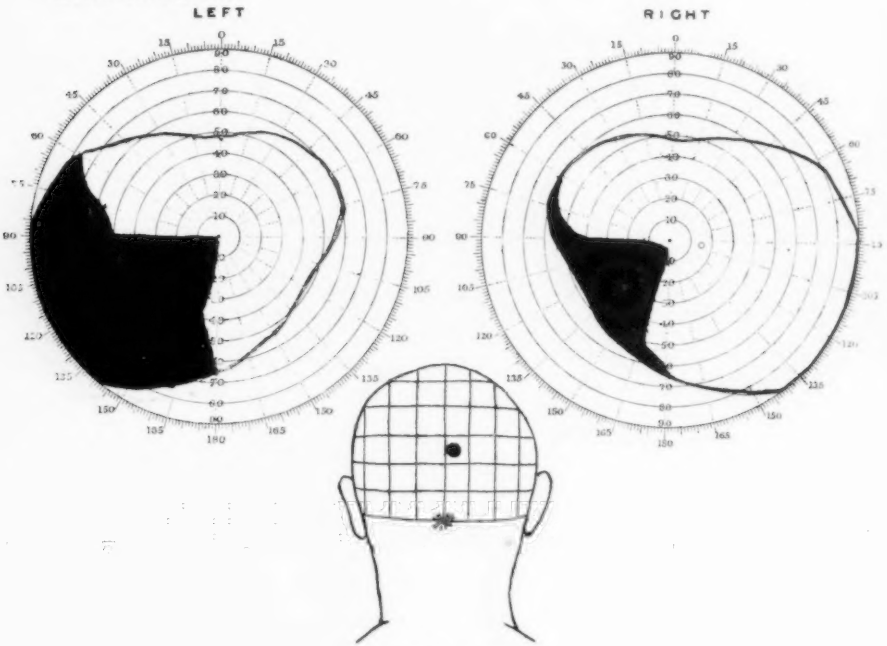

FIG. 5.

Case 4.—Private J., 13,613, was wounded about December 1, 1915, by a bullet. He was unconscious for some days, and, on regaining consciousness, found he was quite blind, but on the next day he could see to the right side. There was no paralysis, sensory disturbance, or reflex changes.

Wound.—The bullet entered in the right lower parietal region $2\frac{1}{2}$ in. (6·5 cm.) above and $1\frac{3}{4}$ in. (4·5 cm.) behind the upper margin of the attachment of the right auricle, and made its exit 2 in. (5 cm.) above the inion and $1\frac{3}{4}$ in. (4·5 cm.) to its left. On his arrival at the base, probably about a week later, small flaps were turned down around both wounds and some depressed fragments of bone removed from the entrance. He made an uneventful recovery. About three weeks after the infliction of the wound his visual fields were carefully examined with test objects 4 mm. in diameter, and it was found

that his vision was limited to the left upper quadrants. The blindness approached to within 3° of the fixation point (fig. 7).

In this case the bullet probably entered in the right angular gyrus, injured the upper part of the right optic radiations beneath it, and, assuming it had gone straight through the skull, it would have passed through the upper part of the right area striata and then entered the left hemisphere through the middle of the area striata, probably near the parieto-occipital fissure.

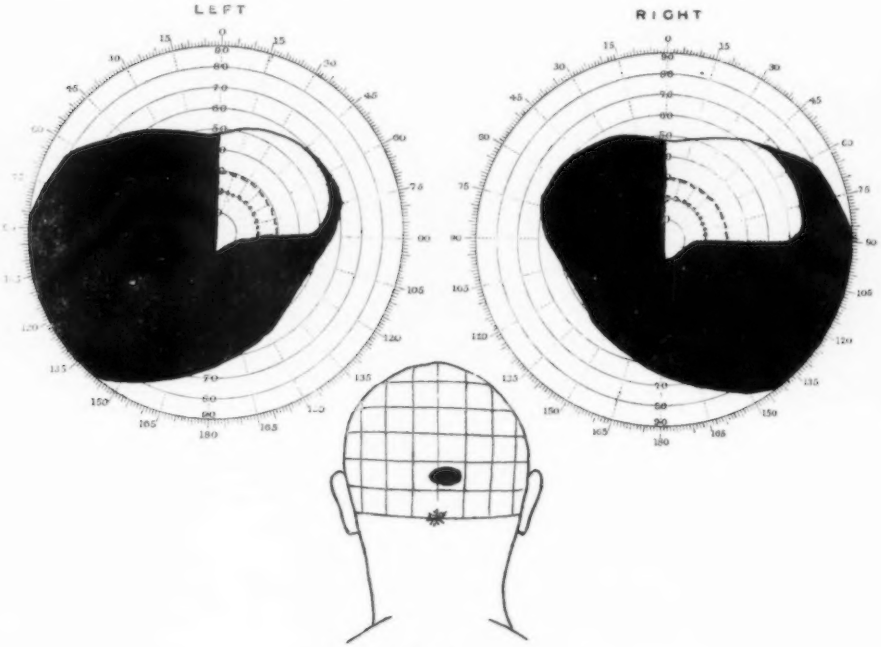

FIG. 6.

We have so far seen only one case of horizontal hemianopia in which the patient's state permitted a careful perimetric examination, but even in this patient there was in addition a superior paracentral scotoma.

Case 5.—Private P., 17,961, was wounded by a rifle bullet on September 25, 1915. He was unconscious for about twelve hours, and thereafter had severe headache and found his sight misty. He arrived at the base three days later.

Wound.—The entrance was a small puncture 3 in. (7·5 cm.) to the left of the middle point of the vertex, the exit being 1 in. (2·5 cm.) above and 1½ in. (3·75 cm.) to the right of the inion. An X-ray examination showed a small entry wound through the skull with a few small fragments of bone driven in,

and a larger blown-out exit wound to the right of and about 1½ in. (3·75 cm.) above the inion. There was then some general weakness of his right arm and of this side of his face, but his legs were equally strong, and the only changes in his reflexes were absence of the right arm-jerks and diminution of the right abdominal reflex. There was also considerable sensory disturbance of the cerebral type in his right upper limb, the appreciation of position, passive movement and form, and the discrimination of compass-points, being lost. The motor symptoms disappeared almost entirely while he was under observation, but some sensory disturbance persisted. His headache was relieved by

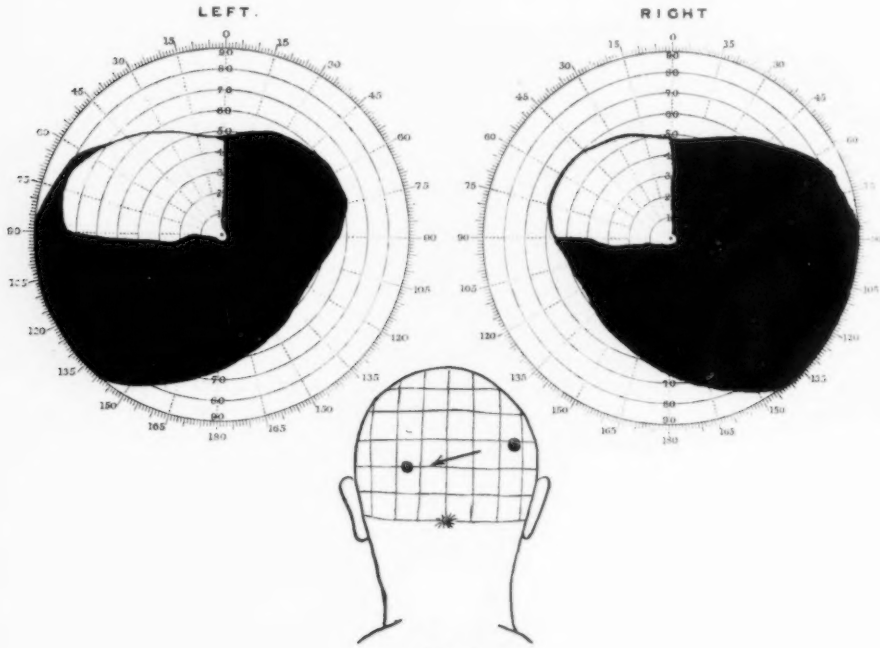

FIG. 7.

lumbar puncture and did not recur. His wounds healed rapidly. When he was first seen, four days after the infliction of the wound, central vision was defective, and he was unable to see below a horizontal line through his fixation point. On October 11, however, central vision was $\frac{6}{6}$ in each eye, and he easily read Jaeger 1, but there was obviously a scotoma to the left of and above the fixation point. A few days later, when he was able to leave his bed, his visual fields were taken carefully and a complete lower horizontal hemianopia, almost limited by a horizontal line through the fixation point was discovered. There was an absolute left superior paracentral scotoma which came

almost up to the fixation point (*see* below) and extended out to 10° (fig. 8). Colour vision was normal at the fixation point and in the superior quadrants, except in the position of the scotoma, where its loss was coterminous with that for white. He remained under observation for five weeks after the infliction of the wound, and during the last three weeks of this period the visual disturbances remained stationary.

In this case the bullet probably entered the left posterior central gyrus at about the level of the superior genu of the fissure of Rolando, passed obliquely backwards, downwards and inwards through this hemisphere in the neighbourhood of or through the upper portion of the sagittal strata, and, from the position of the exit wound, probably cut through the upper part of the right calcarine area and through its posterior extremity at the pole of the hemisphere.

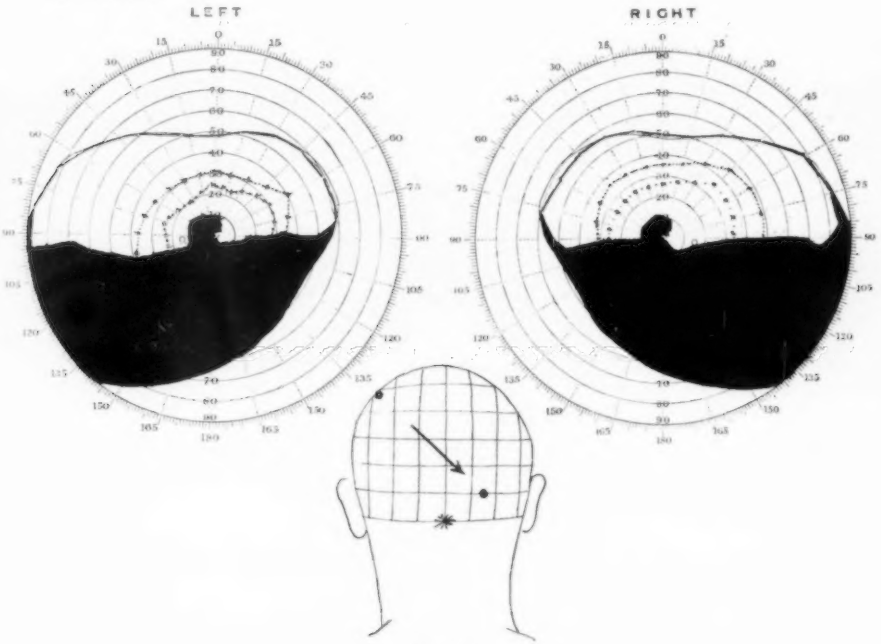

FIG. 8.

It will be noticed that in those cases where one quadrant only was affected it was always the lower quadrant of the visual field, that is, the sector which corresponds to the opposite superior quadrant of the retina, which was blind; this was so in all the cases in which we have observed complete or partial quadrantic blindness. Further, in all cases the

position of the injury or the course of the missile made it probable that the brain was damaged chiefly above the level of the calcarine fissure, and our cases consequently support Henschen's view, for which there is now much evidence, that the upper halves of the retinæ are represented in the upper lips of the calcarine fissures. Inouye's observations on cases injured in the Russo-Japanese War point to the same conclusion.

The rarity of superior quadrantic hemianopia in gunshot injuries of the occipital region is striking; it is probably due to the fact that through-and-through or penetrating wounds in the inferior part of the area striata are liable to produce lesions in the cerebellum, which are notoriously very fatal. The fact that only the upper quadrants on one side escaped in Cases 3 and 4, in which the lesion on the opposite side probably lay above the level of the calcarine fissure, is evidence that the inferior portions of the retina are represented in the inferior parts of the areæ striatæ.

Central Scotomata.

We have had the opportunity of seeing a considerable number of central and paracentral scotomata, and will describe here those cases which bear most definitely on the vexed question of the cortical representation of the macula.

Case 6.—Private F., 2,312, was wounded by a bullet on July 11, 1915. He was unconscious probably for two days, and later had severe headache and found his sight seriously affected.

Wound.—There was a glancing wound across the middle line just above the inion, the entrance being on the right side and slightly above it, the exit on the left and immediately below its level. An X-ray stereoscopic examination showed a grooving of the outer table of the skull at the upper margin of the inion and the depression of a large flake of the inner table on to the poles of both occipital lobes. He was first seen four days after the injury; vision was then much disturbed, but it was not possible to take his visual fields by the perimeter till a week later. Then a large absolute central scotoma, which extended all round the fixation point to about 15°, except below, where it came within the 10° circle, was found. In this area there was complete blindness to white and to colours, the test objects being 2 mm. square. The peripheral fields for both white and colours were unrestricted. (In this and in the following cases, in which central vision was affected, fixation was obtained by placing the tip of the patient's forefinger on the fixation point of the perimeter and making him gaze at it.) He remained under observation for three weeks after the injury; towards the end of this period vision improved to some extent, so

that there was complete blindness only in the upper left quadrants, while over the rest of the scotomatous area there was some, though indistinct, vision (fig. 9).

In this case it was only the tips of the occipital poles which were probably

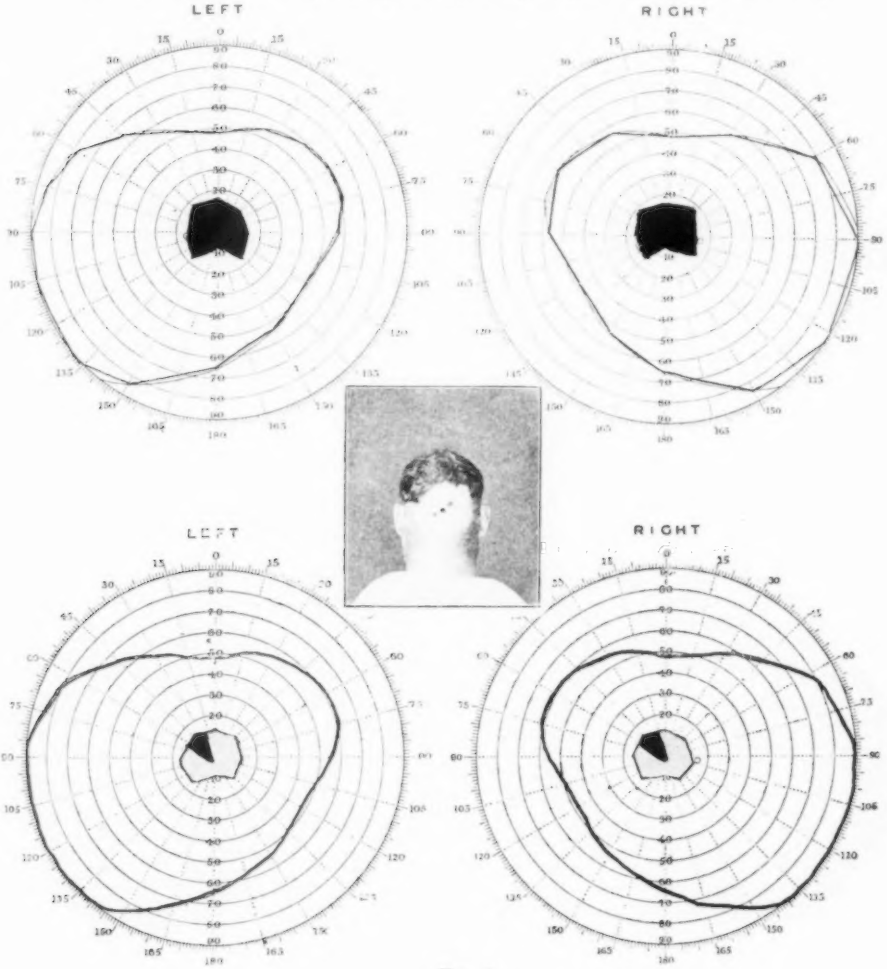

FIG. 9.

injured; they must have been bruised by the depressed portion of the inner table of the skull.

Case 7.—Private R., 1,629, arrived at a base hospital on March 7, 1915. He had been unconscious for some days and could give no history of his injury or of the operation which had been done at a casualty clearing station.

The *entrance wound* was 2 in. (5 cm.) to the left and ½ in. (1·25 cm.) above the level of the inion, while the exit was 2 in. (5 cm.) to its right and 1 in. (2·5 cm.) above its level. There was a small bone defect beneath each wound, through which tense cerebral herniæ protruded. That under the entrance wound did not pulsate. When admitted he had much headache and papillœdema with swelling of 1·5D. to 2D. The right eye was astigmatic and had been amblyopic since infancy, and he had a slight convergent squint.

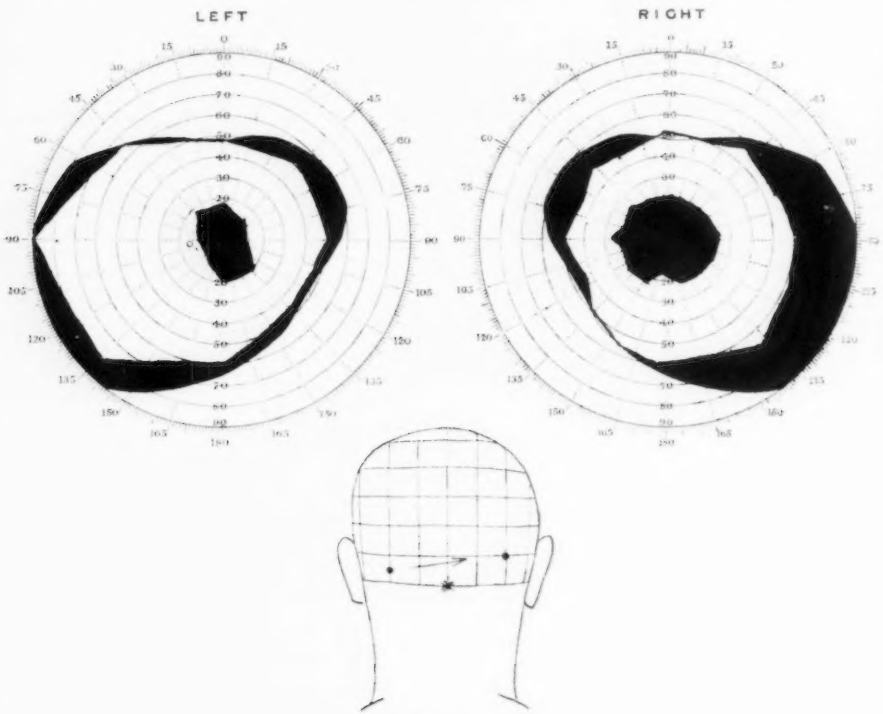

FIG. 10.

Apart from the visual disturbance there were no other symptoms of cerebral injury. His visual fields, taken about ten days after the infliction of the wound, showed a large central scotoma in each eye, which was somewhat more extensive in the right than in the left, and in the amblyopic eye there was also some peripheral contraction, which was probably due to want of attention (fig. 10). The scotomata were practically unaltered when his fields were taken again a few days later and remained so till he was transferred to England.

In this case the wounds were due to a bullet which had passed horizontally across the occipital poles at about the level of the posterior ends of the

calcarine fissures, and which must have consequently destroyed the posterior part of each area striata.

Case 8.—Private L., 8,148, was wounded by shrapnel on March 11, 1915. He was completely blind for two days and had had much headache. There were several shrapnel wounds in the scalp, but the bone was injured only under a triangular wound immediately to the left of the inion. An X-ray examination showed a comminuted fracture in this region with depressed

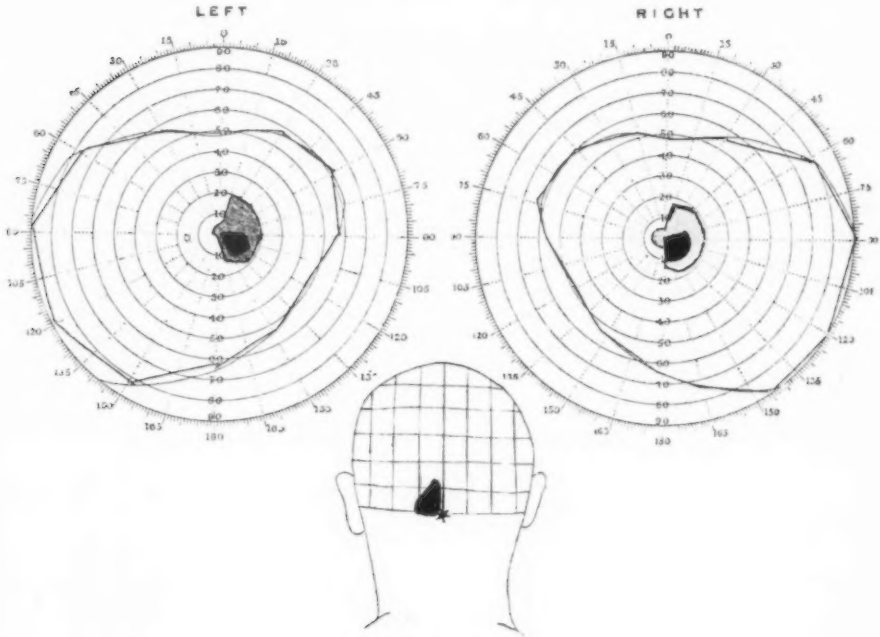

FIG. 11.

fragments of bone in the brain beneath it, and a linear fracture running upwards and outwards to the left parietal eminence. When first seen, four days after the injury, he had complete right hemianopia and some defect of central vision. When his fields were taken eight days later, the peripheral fields were full, but a right absolute paracentral scotoma was discovered which extended outwards to about 20° and inwards to the fixation point. This was surrounded by a partial scotoma which invaded the left halves of the fields to the extent of about 10° round the fixation point. At this time he was unable to read even large letters. Both the complete and the partial scotomata gradually decreased in size, and about three weeks after the infliction of the wound there was only

a small absolute paracentral scotoma in the right lower quadrant, which was surrounded by an area of defective vision. The latter extended to about 5° to the left of the fixation point (fig. 11). At this time he was able to read only the largest letters.

In this case the main injury must have been at the tip of the left occipital pole, but the right occipital pole was probably also damaged to a slight extent.

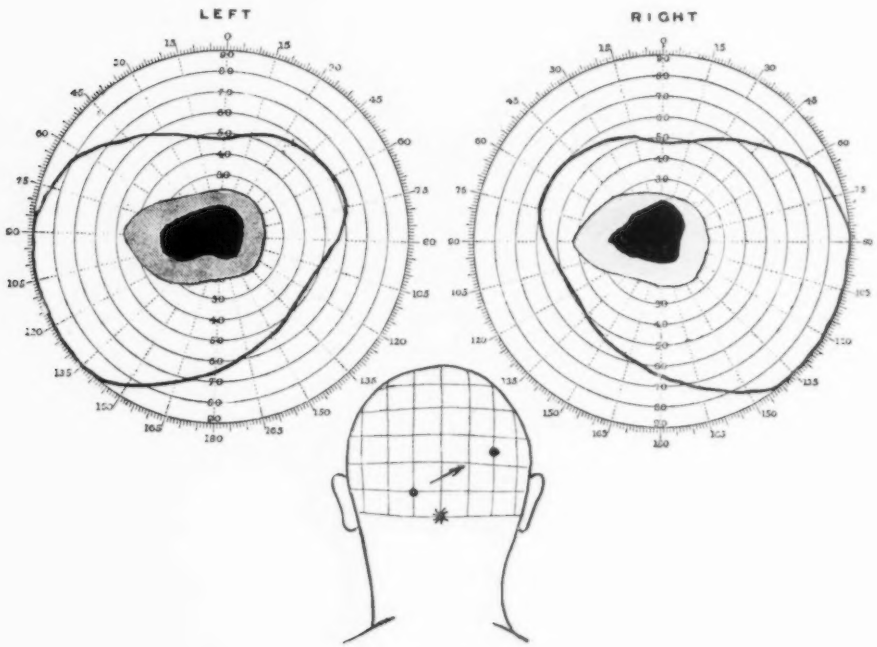

FIG. 12.

Case 9.—Lieutenant T. was wounded on December 20, 1914, by a bullet. He was unconscious for a time, and on coming round found he was quite blind, and had a sensation of positive blackness in front of his eyes. He first noticed, about four days later, the white aprons of the sisters passing by his bed.

Wound.—The entrance lay about 1 in. (2·5 cm.) above the level of the inion and 1 in. (2·5 cm.) to the left. The exit was 2½ in. (6·25 cm.) above the inion and 2 in. (5 cm.) to the right of the middle line. An X-ray plate showed a depressed fracture of the skull and fragments lying in and on the brain. He was operated on by Mr. Hugh Lett on December 23. A

large horseshoe flap, which included the two wounds, was turned down. Brain matter at once escaped from the entrance. The openings in the bone on both sides were enlarged and the intervening bridge of skull removed. The dura had been torn from one opening to the other, and the damaged brain bulged through it after irregular fragments had been removed from both occipital lobes. The patient made an uninterrupted recovery. The visual fields were taken eleven days after injury; there was then a large absolute central scotoma extending about 10° on the right of the fixation point and to nearly 20° on its left. This was surrounded by a zone of partial vision (fig. 12). From this time his sight improved considerably till he was discharged twenty-six days after the injury. There was then very imperfect central vision, with an absolute paracentral scotoma below the fixation point, which was surrounded by an area of incomplete vision. He was now able to recognize large letters. The peripheral limits of the visual fields were unrestricted.

In this case the course of the missile and observation of the injury at the time of operation make it certain that the tip of each occipital lobe was seriously damaged.

Homonymous Hemianopia with Central Scotoma.

Another interesting group of cases that we have observed has been distinguished by the presence of homonymous hemianopia with a central scotoma. In all these the missile, which had an oblique course, caused extensive injury of the occipital lobe or optic radiations of one side, and passed through or near to the tip of the occipital pole of the opposite hemisphere.

Case 10.—Private G., 10,634, was probably injured on March 26, 1915, by a rifle bullet. He was completely blind for two or three days, and then began to distinguish light to the left side. He was admitted to a base hospital five days later. He had been operated upon in the casualty clearing station on the day following the injury. He was at first very drowsy and had some difficulty in understanding speech, but this rapidly cleared up.

Wound.—The entrance was 2 in. (5 cm.) above and 1½ in. (3·75 cm.) to the right of the inion. The exit was represented by a large circular defect in the scalp about 1½ in. (3·75 cm.) to 2 in. (5 cm.) in diameter, through which softened and disintegrated brain protruded. Its centre was 2½ in. (6·25 cm.) above and 1½ in. (3·75 cm.) to the left of the inion. An X-ray photograph showed a large bone defect under the exit wound, which reached to the middle line and extended almost down to the inion. There was no paralysis or sensory disturbance, and his reflexes were normal. At first he had vision only in the left upper quadrants, but later vision returned in the whole periphery of the left visual field, but a large central scotoma extending to about

20° to the left of the fixation point persisted till he was transferred to England, a month after the infliction of the wound (fig. 13).

In this case there can be no doubt that the posterior part of the optic radiations of the left hemisphere, and probably a considerable part of the calcarine cortex, were destroyed by the missile and by the secondary changes involved in the hernia formation, while on the right side the bullet merely passed through the posterior extremity of the occipital lobe.

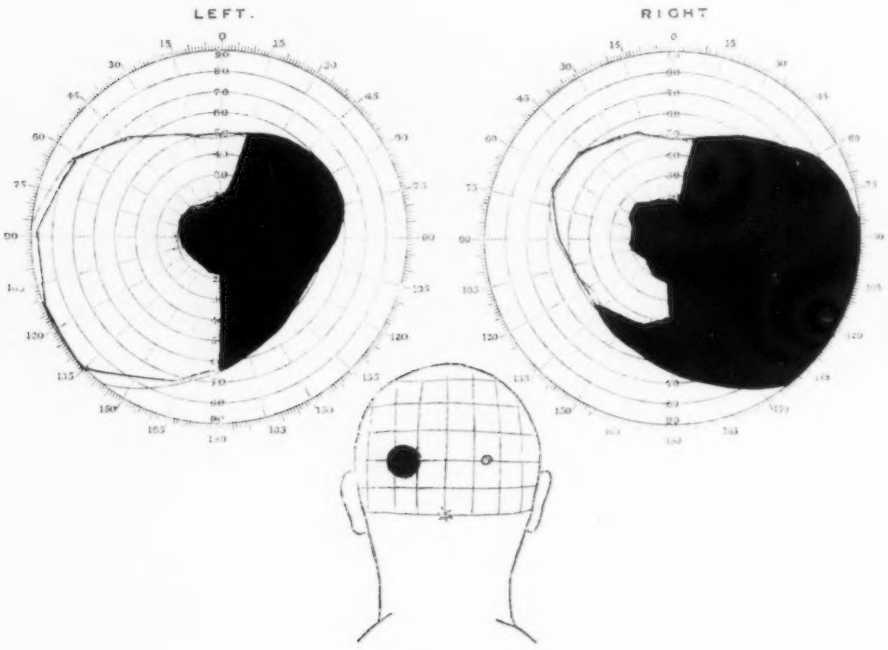

FIG. 13.

Case 11.—Private M., 1,424, was wounded by a rifle bullet on September 25, 1915. He was blind for the first two days and had a sensation of blackness in front of his eyes. He reached the base three days later, and then presented no abnormal symptoms apart from visual disturbance.

Wound.—The entrance was 2 in. (5 cm.) above and 3 in. (7·5 cm.) to the left of the inion. The exit was 2 in. (5 cm.) to the right and 2 in. (5 cm.) above the inion. An X-ray photograph showed under the entrance wound a defect in the skull at the lambdoid suture, with many fragments of bone driven into the brain, while the exit was represented by a blown-out wound to the right of and slightly above the inion. The visual fields, taken three weeks after

injury, showed complete right-sided homonymous hemianopia and a central scotoma which extended to just beyond 10° to the left of the fixation point (fig. 14). His vision remained in this state till he was transferred to England.

In this patient the injuries were similar to those in Case 10. The left optic radiations must have been injured by the depressed fragments of bone and by softening under the wound of entry, while owing to the oblique course of the missile it is probable that only the posterior extremity of the hemisphere was damaged on the right side, and chiefly on its mesial surface.

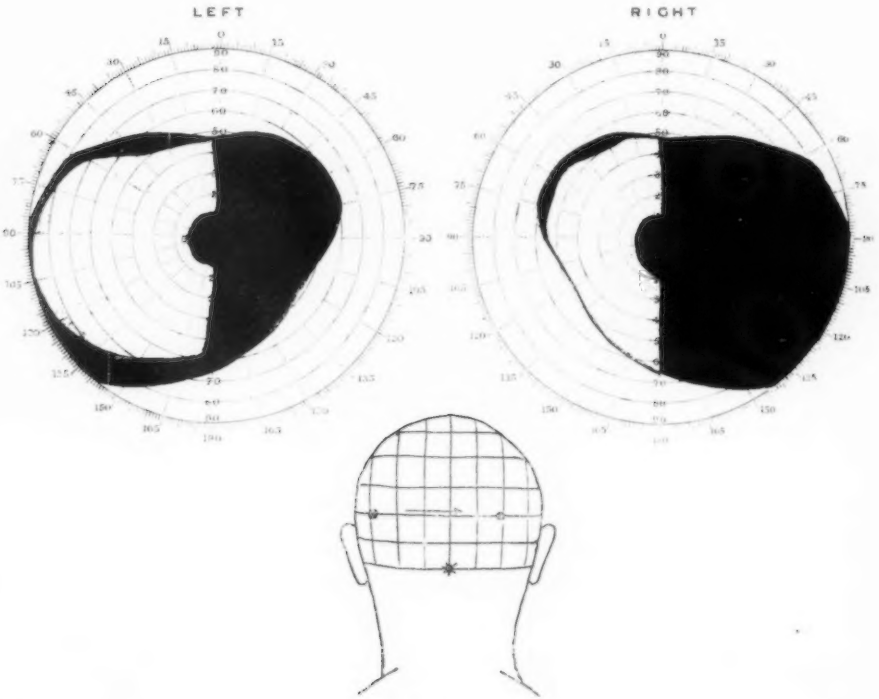

FIG. 14.

Case 12.—Private M., 16,694, was admitted to a base hospital on January 13, 1916. He was then quite blind, but a few days later could recognize light in the left periphery of his visual fields.

Wound.—The entrance was 1½ in. (3·75 cm.) above and 3½ in. (9 cm.) to left of the inion; exit 1½ in. (3·75 cm.) above and 1½ in. (3·75 cm.) to right of the inion. An X-ray photograph showed fragments of bone driven into the brain beneath the entrance wound. There was no paralysis, sensory or speech

disturbances, or alteration in his reflexes. The depressed fragments of bone with some disintegrated brain were later removed from the wound of entrance, but owing to the spread of infection to the ventricle and the occurrence of meningitis, he died five weeks after the infliction of the wound. The visual loss was so extensive that it was never possible to take his visual field with a perimeter, but during the whole time he was under observation he had complete right homonymous hemianopia with an absolute central scotoma, which extended for about 20° to 30° to the left of the fixation point. At the autopsy a large septic wound was found in the left occipital lobe, which involved all the structures lateral to the ventricle, including the optic radiations. On the right side the bullet had, in passing, destroyed about the posterior third of the calcarine cortex (fig. 15). The brain was not infected on this side, and the rest of the area striata was undamaged.

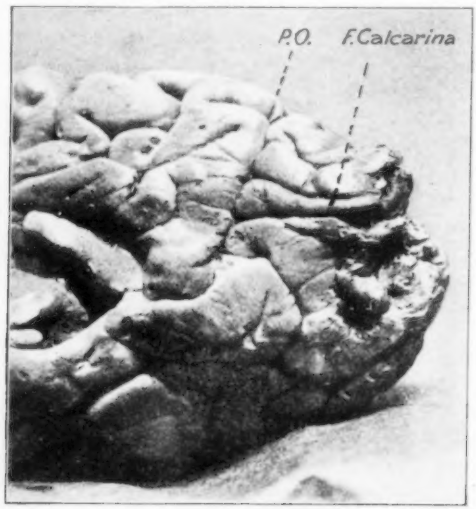

FIG. 15.—Photograph of mesial surface of the right occipital lobe in Case 12, showing superficial damage at the posterior extremity of the calcarine fissure.

In these seven cases (Cases 6 to 12), there were absolute central scotomata of various sizes. In the first four peripheral vision was unaffected, but in Cases 10, 11, and 12 the central scotomata were associated with homonymous hemianopia.

In those cases in which there was a pure central scotoma the lesion was, as far as it is possible to judge from the course of the missile, from the evidence afforded by radiographic examination, and from the conditions found at operation, limited to the posterior ends of the occipital

lobes at or about the level of the posterior extremities of the calcarine fissures. Consequently it is probable that only the hindermost ends of the areæ striatæ were damaged. This was obviously so in Cases 7 and 9, while in Case 6 the depression of the inner table must have bruised and probably produced softening of the occipital poles. In Case 8 the cranial injury, it is true, was unilateral, but it is the common experience that such depressed fractures due to shrapnel or fragments of shell-casing often produce relatively diffuse damage; further, in this case the visual symptoms diminished rapidly, so that when he was last examined the absolute scotoma was only paracentral; its position in the right halves of the visual fields corresponded with complete functional abeyance of a portion of the left area striata, and it was over the posterior part of this that the lesion actually lay.

These observations, associated with the fact that among over 2,000 cases of head injury we have never seen a central scotoma when a direct injury of the occipital poles could be excluded, afford strong evidence that central vision is represented on either the mesial or the lateral surface of the poles of the occipital lobes. Further, our observations conform to the generally accepted view that the visual area corresponds with, or at least includes, the area striata.

Those cases (10, 11, and 12) in which there was a homonymous hemianopia in addition to a central scotoma also conform to or support this view. In Cases 10 and 11 the hemianopia was probably due to the extensive lesions on the lateral surfaces of the occipital lobes on one side, which involved the optic radiations, while, owing to its oblique course, the missile can have injured directly only the posterior pole of the opposite hemisphere. In Case 12, in fact, in which the visual fields were, as far as could be ascertained by rough methods of examination, very similar to those of the two preceding cases, the optic radiations and the greater part of the calcarine cortex were destroyed on the left side, while in the right hemisphere the destruction involved only the posterior part of the area striata; and this lesion corresponded with loss of central, but with intact peripheral vision in the left halves of the visual fields.

It is true that in all such lesions afferent sensory tracts must be damaged in addition to the cortex, but as the fibres of the optic radiations destined for the anterior extremity of the area striata do not extend farther posteriorly than the horn of the ventricle (fig. 3), it can be assumed that when the lesion is limited to the occipital pole centripetal fibres to this region only are involved.

The evidence so far consequently points to representation of the macula at the posterior pole of the hemisphere. This conclusion is strongly supported by the next group of visual disturbances with which we shall deal.

Paracentral Scotomata.

We have seen a considerable number of cases with paracentral scotomata—that is, isolated areas of blindness in the visual fields which lie to one side of the fixation point, but do not involve it.

Case 13.—Private B., 416,152, was wounded by a round shrapnel bullet. He was unconscious for some time, and his state on admission made it impossible to obtain an accurate history.

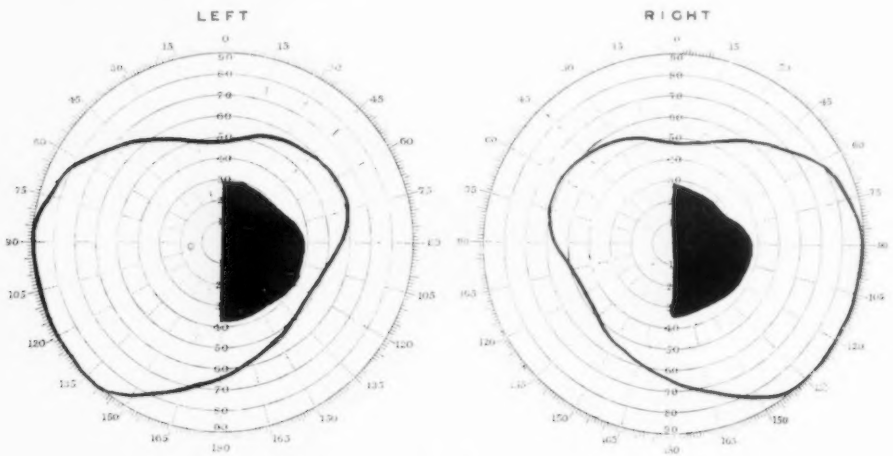

Fig. 16.

Wound.—The entrance was immediately below the inion in the middle line, and an X-ray photograph showed the bullet immediately inside the skull at the base of the left mastoid process. It was removed from this position the next day. An extensive injury of the left lateral lobe of the cerebellum was discovered. The occipital lobes were not examined, but the bone was widely fractured over the pole of the left hemisphere. Recovery was uninterrupted. When he was first examined, he had probably a right hemianopia, but his state did not permit a thorough examination. Four weeks later, however, when he was able to sit up, only a paracentral scotoma to the right of the fixation point was discovered. It extended from the fixation point, both above and below the horizontal level, and outwards to about 30° (fig. 16).

In this case the exact extent of the injury of the visual area was not determined, but probably its posterior part was most seriously damaged.

Case 14.—Private B., 13,426, was wounded by a piece of shell-casing on February 3, 1916. For an hour or so he had a "dim mist" in front of his

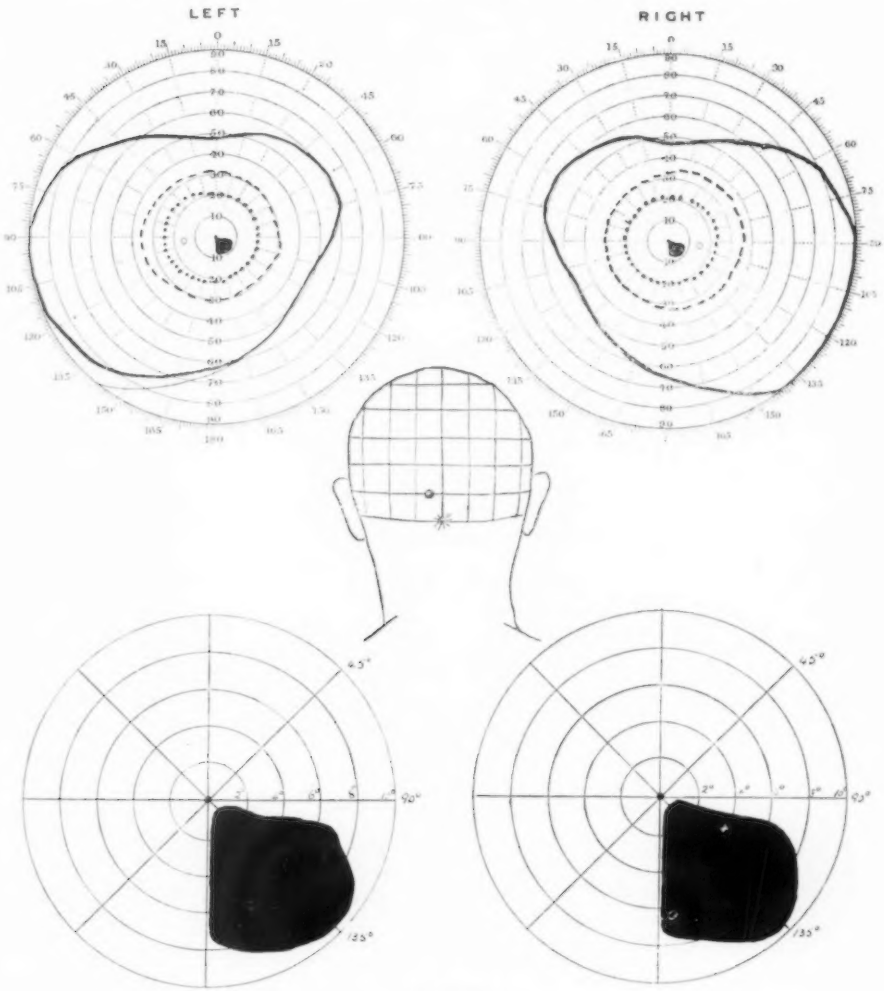

FIG. 17.

eyes, but this gradually disappeared, and when he was admitted to the base hospital two days later he was unaware of any defect in sight.

Wound.—A small contused scalp wound, the centre of which was 1 in.

(2·5 cm.) above and ½ in. (1·25 cm.) to the left of the inion. An X-ray photograph showed a narrow crack in the outer table and a small depression of the inner table immediately under the wound. The scalp wound was excised, but the skull was left untouched. When the visual fields were taken, twelve days after the infliction of the wound, the limits to those for white, red, and green were unrestricted, but there was a small absolute scotoma in the right inferior quadrant which reached to within 1° of the fixation point, and extended outwards

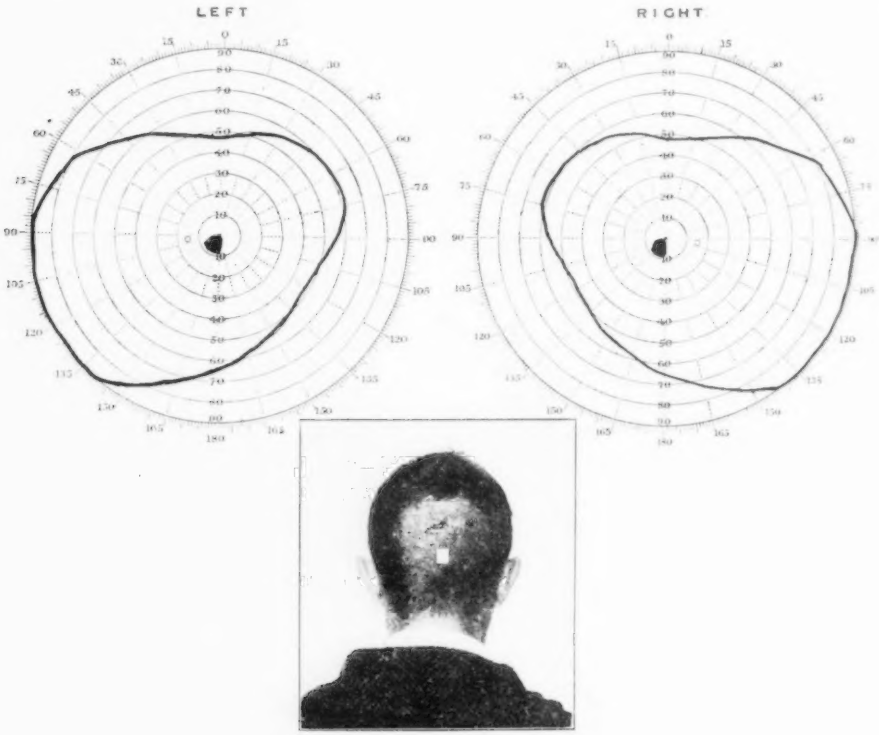

FIG. 18.

to 10° (fig. 17). The areas over which perception of white and that of colours were lost were identical.

The position of the wound and the X-ray examination make it probable that in this case there was a contusion of the left occipital pole at the upper lip of the calcarine fissure.

Case 15.—Lieutenant H. was wounded on November 5, 1915, by a bullet. He noticed at first he could not see his feet, but his vision improved rapidly,

and when he was first seen by us four days later, his only complaint was that on attempting to read he could not see the four or five lines immediately below that which he was reading, though the rest of the page was visible to him.

Wound.—A tangential scalp wound with its entrance 1 in. (2·5 cm.) above and $1\frac{1}{2}$ in. (3·75 cm.) to the right of the inion, while the exit was in the middle line and $\frac{1}{2}$ in. (1·25 cm.) above the inion. An X-ray photograph showed no definite changes in the skull. Examination of visual fields revealed a small absolute paracentral scotoma for white and colours which lay chiefly in the left lower quadrants; it extended up to the fixation point and downwards and outwards to about 9 (fig. 18). This condition remained unaltered three weeks after the infliction of the wound.

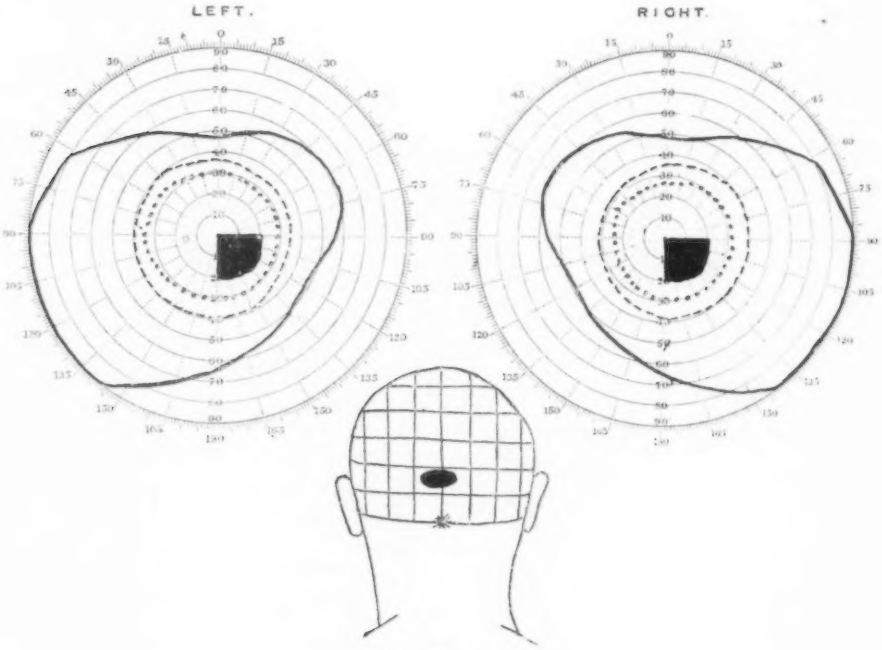

FIG. 19.

In this case the wound lay immediately above the posterior extremity of the upper lip of the right calcarine fissure.

Case 16.—Private A., 17,385, was wounded on February 12, 1916, by a piece of shrapnel. He did not become unconscious, but noticed his sight affected immediately. He was operated upon at a casualty clearing station on the following day, when a depressed fracture of the occipital bone was found over the longitudinal sinus. The dura was probably undamaged. When

admitted to the base five days later there was a transverse wound across the middle line $1\frac{3}{4}$ in. (4·5 cm.) above the level of the inion, and an X-ray photograph revealed a defect in the skull midway between the inion and lambda in the middle line. Perimetric examination showed that the peripheral limits of white and colours were unrestricted, but there was an absolute scotoma for both white and colours in the right lower quadrants which extended from the fixation point to about 20° outwards and downwards (fig. 19). His central vision was $\frac{6}{9}$ in each eye.

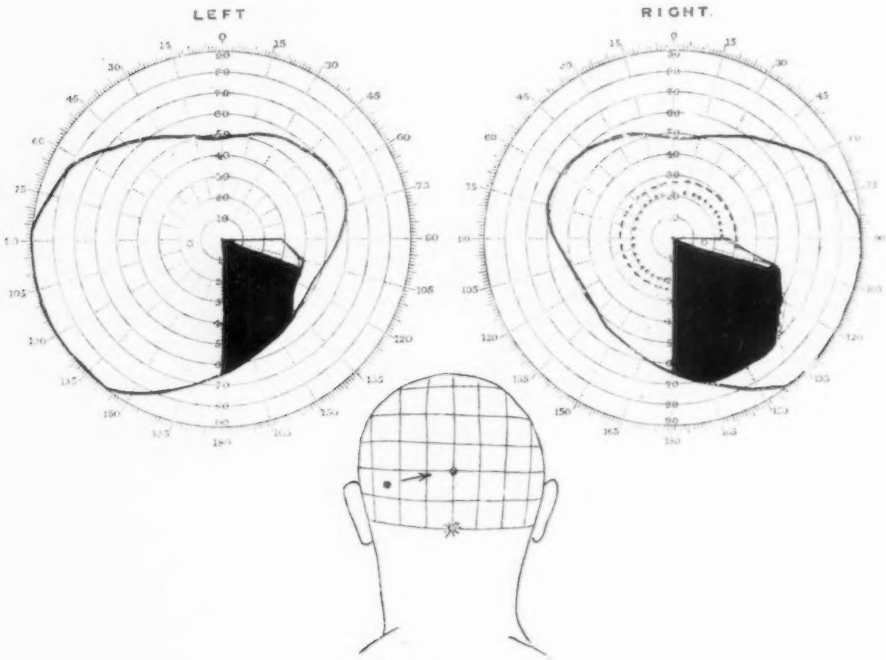

FIG. 20.

Case 17.—Lieutenant F. was wounded March 13, 1915, by a bullet. His sight at once became indistinct. Two days later he was operated upon at a casualty clearing station.

Wound.—Entrance was $1\frac{1}{2}$ in. (3·75 cm.) above and $2\frac{1}{2}$ in. (6·25 cm.) to the left of the inion. The exit was in the middle line and 2 in. (5 cm.) above the inion, and they were joined by a healed incision, beneath which a defect in the skull could be felt. Perimetric examination was first made a fortnight later. He then had a complete scotoma for white and colours in the right inferior quadrants which reached from the fixation point to the limit of the

normal field immediately below; but to the right of this there was peripheral vision to both white and large areas of colour, which shows that the defect in the field was of the nature of a paracentral scotoma rather than a quadrantic loss (fig. 20). At the upper border of the scotoma the blindness was only partial from the horizontal line to 15° below it.

In this case the extent of the damage was uncertain, but the wound lay over the upper and posterior portion of the left area striata.

Case 18.—Sergeant D., 16,197, was wounded by a fragment of a high-explosive shell on March 2, 1916. He was dazed for a moment, but not unconscious, and noticed at once "stars and very brilliant revolving things" in front of his eyes, whether they were open or closed; when he arrived at

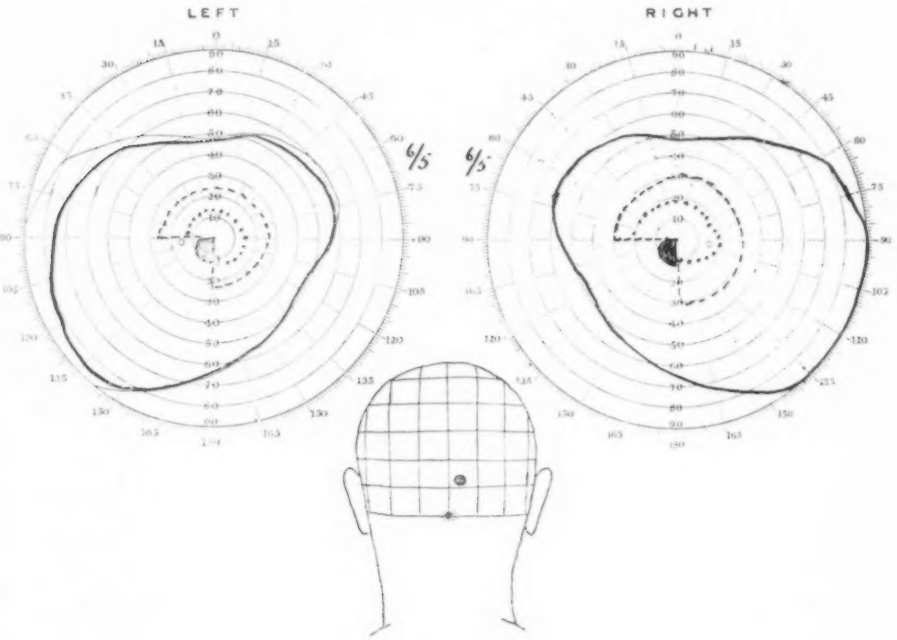

FIG. 21.

the base, he was unable to say if these visual spectra had appeared more to one side than to the other. It seemed to him, too, that there was a mist in front of his eyes, but his vision improved rapidly.

The wound was a small gaping incision 1¼ in. (slightly more than 3 cm.) above the inion, and slightly to the right of the middle line. This was explored next day, and a small depressed fracture, in which a piece of metal was

impacted, was found immediately to the right of the longitudinal sinus and 1¼ in. (slightly more than 3 cm.) above the apex of the inion.

His visual fields were first taken three days after the infliction of the wound, and again three weeks later. On each occasion a small paracentral absolute scotoma, which extended up to the fixation point, was found in the left lower quadrants; vision for red and green was lost beyond this, and vision for white objects 5 mm. square was indistinct. Otherwise there was no peripheral restriction of vision for white or colours (fig. 21). His central vision after correction was $\frac{6}{5}$ in each eye

The exact position of the depressed fracture was carefully measured in this case at the time of operation, and its position was found to correspond with the posterior extremity of the upper lip of the calcarine fissure.

Case 19.—Private C., 12,993, was wounded by a rifle bullet on January 5, 1916. He was unconscious for two hours, and then found his sight much affected; it rapidly improved, however.

Wound.—The entrance was 2 in. (5 cm.) to the left, ½ in. (1·25 cm.) above the inion; exit 1 in. (2.5 cm.) to the right and slightly lower than the inion. An X-ray examination showed a medium-sized entry wound in the skull with depressed bone beneath it, and an exit with out-driven bone immediately to the right of the inion. Two days after arrival at the base he was operated upon. A horse-shoe flap was turned down, and it was seen that the entrance lay just above the lateral sinus on the left side. This was firmly thrombosed. A large flake of bone was removed from the brain and several small pieces, as well as a firm clot from the upper margin of the cerebellum. He made a rapid recovery. His visual fields were first examined three weeks after infliction of the wound. There was an absolute paracentral scotoma in the right upper quadrants which extended from the fixation point outwards to 20°, and projected slightly below the horizontal. This was surrounded by an area of partial scotoma, in which white was dull and indistinct, and colours not recognized with certainty. The peripheral limits of the fields for white and red were unrestricted, but green objects of 10 mm. square could not be recognized to the right of the scotoma. The absolute scotoma, when measured by Bjerrum's screen, was found to extend up to less than 1° of the fixation point (fig. 22). His visual acuity was, however, $\frac{6}{9}$. The only complaint of vision he made was that in reading he had occasionally lost his place. His visual fields were repeatedly taken, but remained unaltered till he left for England six weeks after the infliction of the wound.

There can be no doubt that in this case the occipital pole was injured chiefly below the extremity of the left calcarine fissure.

Case 20.—Private T., 868, was wounded on March 6, 1916, by a fragment of shell. He was unconscious for a short time, but apart from some headache he was not aware of any abnormal symptoms. He arrived at the base two days later.

Wound.—There was an irregular gaping wound about ½ in. (1·25 cm.) above

the apex of the inion and immediately to the left of the middle line. The bone was exposed and was seen to be fractured and depressed. An X-ray examination showed that the skull was comminuted and depressed immediately

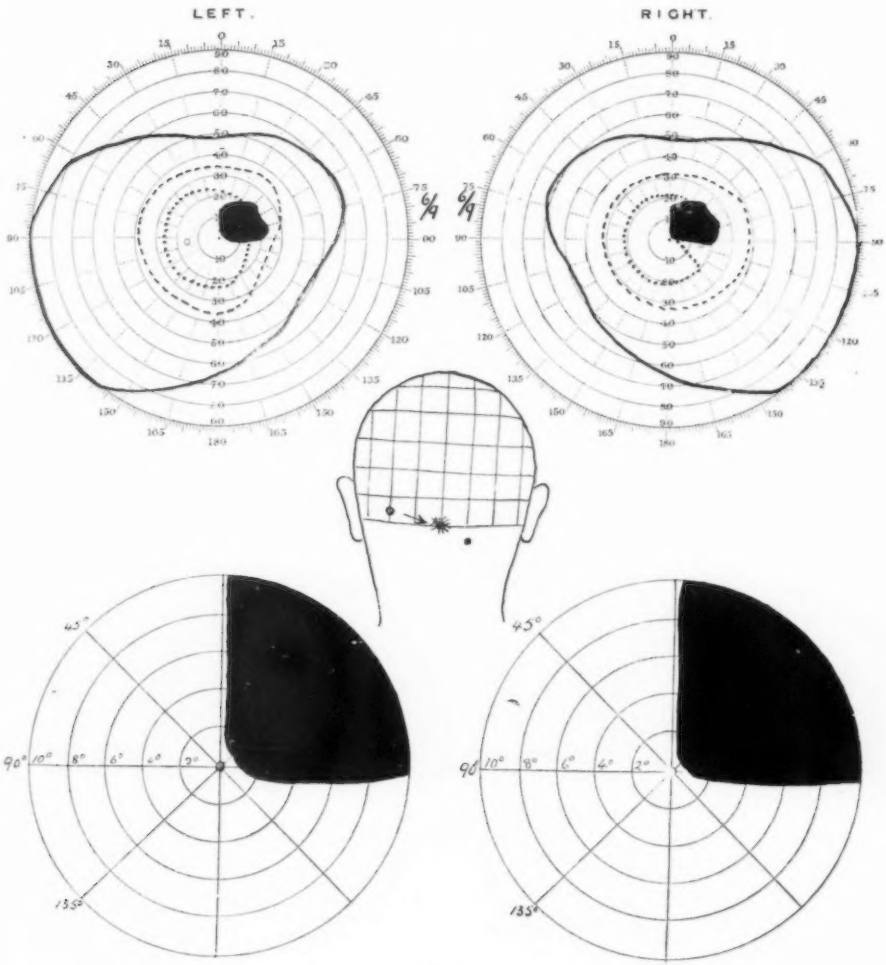

FIG. 22.

above the level of the internal occipital protuberance. When first seen his vision was $\frac{6}{12}$ in each eye, and he was unaware of any disturbance of vision, but examination revealed a small paracentral scotoma in the right upper quadrant, which extended to the fixation point.

A few days after admission to hospital, a flap was turned down over the occipital pole, and then a crater-like depression was seen in the skull, the centre of which was immediately to the left of the middle line and about $\frac{1}{3}$ in.

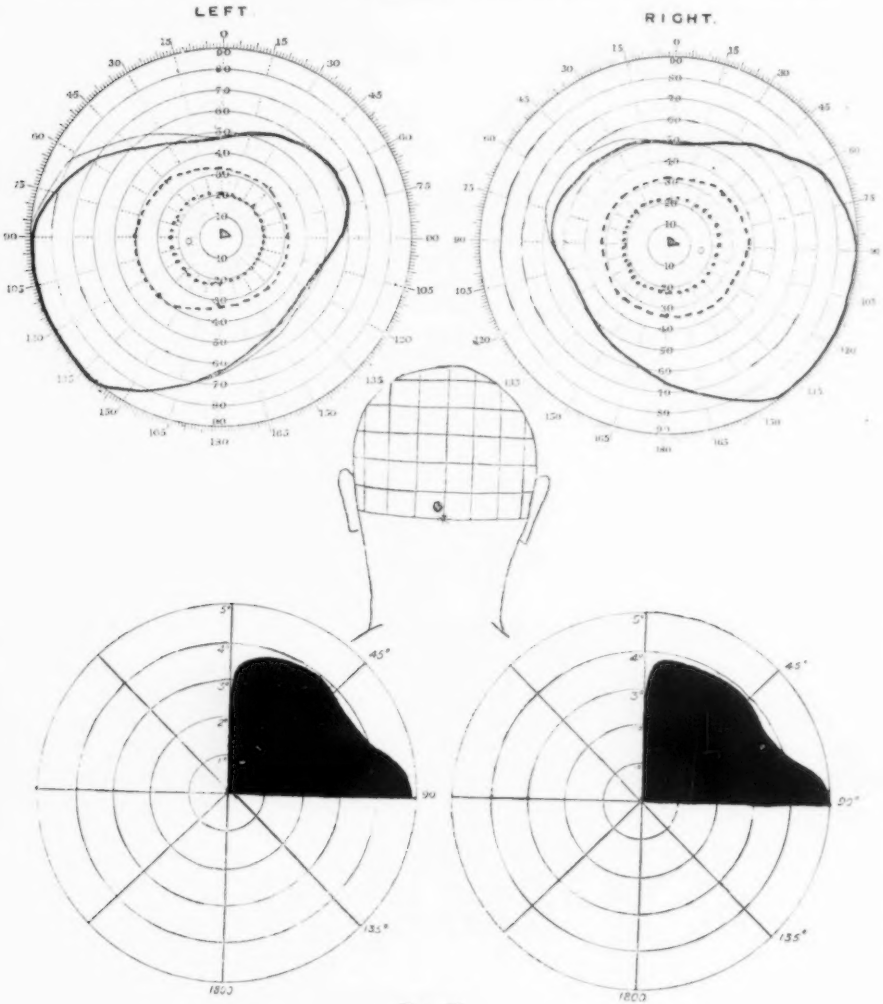

FIG. 23.

(about 0·75 cm.) above the inion. In order to remove the depressed bone, a trephine opening was made to the left of it, and it was there found that a large area of the inner table which had been driven in had lacerated the left lateral

sinus and bruised the inferior surface and the tip of the left occipital pole. The wound healed rapidly. He remained under observation till five weeks after the infliction of the injury.

His visual fields were repeatedly examined, but remained practically unchanged. The peripheral limits of the fields for white, red and green (objects 5 mm. square) were normal, but, as above mentioned, there was a small paracentral scotoma in the right superior quadrant which extended from the fixation point to about 5° outwards. The perception of colours was lost over the same area (fig. 23). He was not aware of this defect and could read quite well. His central vision five weeks after the infliction of the wound was $\frac{6}{9}$ in each eye.

In this case it was definitely determined at the operation that the left occipital lobe was injured at the posterior and inferior aspect of its pole.

Case 21.—Lance-Corporal G., 2,541, was wounded by a bullet as he was bending forward on January 26, 1916. He was unconscious for half an hour or so, and afterwards noted his sight was slightly affected.

Wound.—There was a long oblique wound which extended from the middle line of his skull about 2 in. (5 cm.) above inion, downwards and to the left for a distance of $2\frac{1}{2}$ in. (6·25 cm.). On separating the edges of the wound a narrow gutter defect was found in the skull through which disorganized brain protruded. An X-ray examination showed a large flake of bone driven into the left occipital pole. Three days after the injury the depressed bone was removed and some softened brain washed away. His head wound healed rapidly. The bullet had also passed through the posterior part of his left shoulder. His fields were first carefully examined by the perimeter one month after the injury. There was found a large paracentral scotoma, which extended from the fixation point into the right halves of the fields to the extent of 20° to 30°, and in the lower portion of the left halves of the fields to the extent of 25° (fig. 24). The peripheral limits of vision for white were normal, but green and red objects 10 mm. in diameter were visible only to the left of the vertical line. Examination by Bjerrum's screen showed that the blindness extended to less than $\frac{1}{4}$° from the fixation point. His visual acuity was $\frac{6}{6}$ in each eye. His fields were taken repeatedly, but remained practically unaltered till he left for England six weeks after his injury was inflicted.

In this case the left occipital pole, both above and below the level of the calcarine fissure, must have been extensively damaged, while the right hemisphere was probably injured at the level of the upper part of the wound by the in-driven flake of bone, which had probably penetrated the falx cerebri. The exact extent of the lesion could not be accurately determined at operation.

In these nine cases the paracentral scotomata, of various sizes appeared on ordinary perimetric examination to reach immediately to the fixation point, and on more careful investigation by a Bjerrum's screen they were found to come within at least 1° of it. If the fovea centralis subtends an angle of 4° to 6° (Starling), vision subserved

by it would be consequently involved. In these cases the lesions were in all probability relatively superficial, except in Case 17, and in all

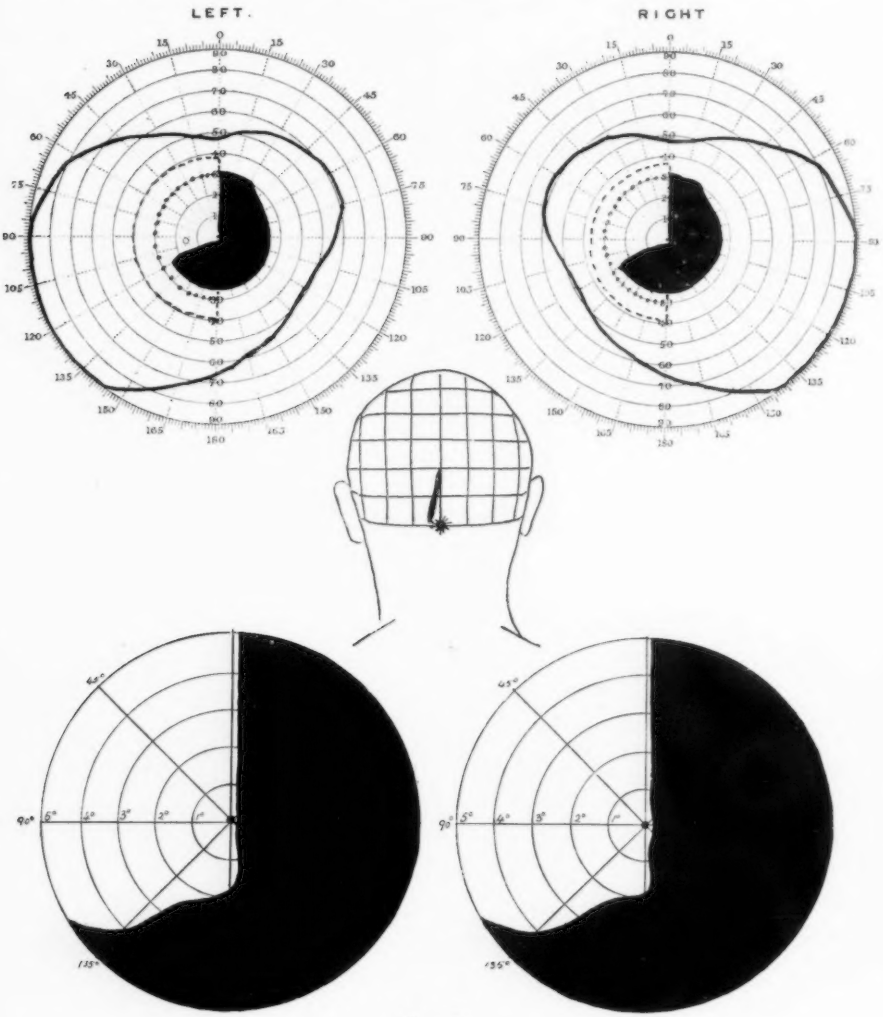

FIG. 24.

they lay over or in the neighbourhood of the posterior extremity of the one calcarine fissure. They consequently support the conclusion already

put forward that central vision is represented in the posterior parts of the occipital lobes. Further, it will be observed that in Cases 14 to 18, in which the paracentral scotomata were limited to the lower quadrants of the visual fields, the main lesions probably lay above the level of the posterior extremity of the calcarine fissures; this fact consequently confirms the conclusion that the upper half of each retina is represented in the dorsal part of the area striata. Cases 19 and 20 are the only two we have yet seen with superior paracentral scotomata; in these the brain was damaged on the under surface of the pole, and it is consequently evidence that those portions of the lower quadrants of the retina in the neighbourhood of the fovea are represented in the lower and posterior parts of the areæ striatæ.

In Case 21, in which we found a triquadrantic scotoma, the whole breadth of the posterior part of the visual cortex was probably destroyed on the left side. The defect in the left visual field, which, it will be noticed, did not reach the fixation point, was probably due to an injury of the mesial surface of the right hemisphere.

We can consequently conclude that not only is central vision represented towards the posterior part of the occipital lobe, but also that the upper portion of the retina in the immediate neighbourhood of the macula corresponds with the upper and most posterior part of the area striata, while the central portion of the retina below the level of the macula is represented in its lower and posterior part.

It is obviously impossible to draw definite conclusions from material such as ours, since our clinical observations have not been controlled by anatomical examinations, but we can suggest tentatively that the portion of the area striata which extends to the margin and on to the lateral surface of the occipital lobe is the cortical focus of central vision. For in the first place, in all the scotomata we have observed associated with injury to this region the blindness involved, or reached to within 1° of the fixation point, though their sizes varied considerably; in other words, the fixation point or its immediate vicinity was that portion of the visual field which was constantly affected by posterior occipital lesions.

In the second place, in such cases as 6, 14, 15 and 18 the depression of bone upon, or the effects of concussion immediately over, the posterior aspect and the lateral surface of the occipital lobe produced a local disturbance of vision which extended up to or involved the fixation point.

Again, if the macula is represented on the posterior aspect of the

hemisphere we should expect that wounds which penetrate the occipital lobe at the level of the extremity of the calcarine fissure would produce homonymous blindness reaching to the fixation point, and this we have actually found to be the rule. The following case illustrates it:—

Case 22.—Lieutenant C. was wounded by a bullet May 9, 1915. He was unconscious for some time and could give no history. When admitted to the base hospital three days later he was very dull and could recognize objects only to the right of the fixation point.

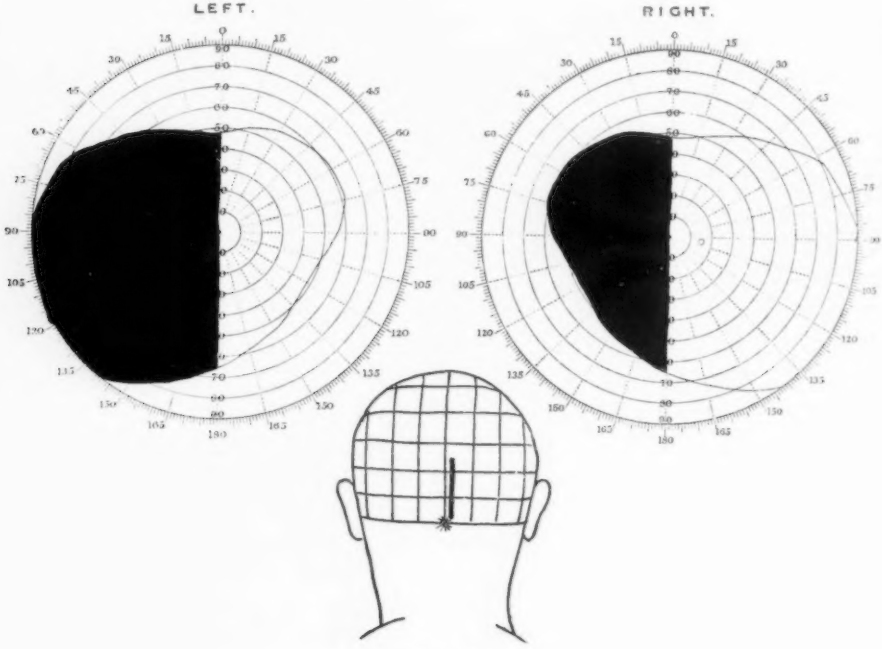

FIG. 25.

Wound.—There was a gaping gutter wound on the right side, parallel and close to the middle line, which extended from the inion 2½ in. (6·25 cm.) upwards. X-ray examination showed a linear defect in the skull and several pieces of bone driven deeply into the brain. An operation was performed the next day; a hole in the skull 2 in. by ½ in. (5 cm. by 1·25 cm.) was found; the dura was lacerated for 1 in. above the inion and immediately to the right of the longitudinal sinus. Disintegrated brain protruded through it. Fragments of bone were removed from a long track, which passed directly forwards to a

depth of about 2 in. (5 cm.). There was considerable destruction of brain around the track. A perimetric examination was made two weeks after infliction of the wound; he had then complete left hemianopia extending right up to the fixation point (fig. 25).

But any such hypothesis on the cortical localization of central vision must be capable of explaining all generally accepted facts. The most important of these is the frequent escape of macular vision in homonymous hemianopia due to vascular occlusion. The explanation probably depends on the vascular distribution in the region of the occipital

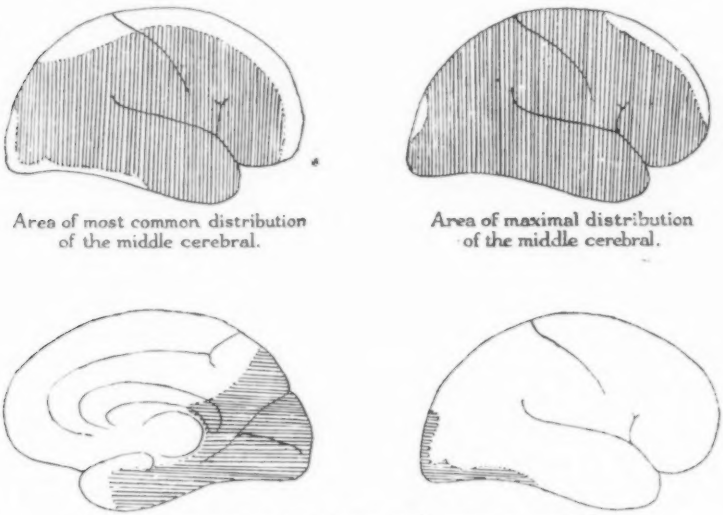
Area of most common distribution of the middle cerebral.
Area of maximal distribution of the middle cerebral.
Area of most common distribution of the posterior cerebral.
(from Beevor)

FIG. 26.

pole. According to Beevor's classical work on the distribution of the cerebral vessels, the occipital pole is usually supplied by the posterior cerebral artery, but the middle cerebral extends usually to within $\frac{1}{2}$ in. to $\frac{1}{4}$ in. (1·25 cm. to 0·7 cm.) of it, and occasionally actually includes it (fig. 26). The occipital pole, and particularly its lateral aspect, is consequently a watershed area between these two large vessels; it may under normal conditions draw blood from both, and if one is blocked the other may suffice to maintain its nutrition. It is, in fact, well known that the softening due to occlusion of any cortical artery is rarely as extensive as its anatomical distribution. If this view is correct the presence or

absence of macular escape in hemianopia due to vascular lesions may be explained by the varying degree of anastomosis between, and the relative extent in the distribution of, the posterior and the middle cerebral arteries at the occipital pole of the hemisphere. The frequent persistence of central vision in bilateral hemianopia due to bilateral cortical lesions may be possibly explained by this same fact.

To make our conclusions complete it would be necessary to bring forward evidence on the cortical representation of peripheral vision. If the macular centre lies in the posterior part of the area striata, and if, as we find, lesions here do not affect peripheral vision, it might be assumed that the latter is represented in the more anterior part of the visual zone; and the fact that the size of the scotoma, whether central or paracentral, varies directly with the depth of the wound from the occipital pole, makes it probable that the concentric zones of the retina from its centre outwards are represented in serial order from behind forwards in the visual area.

We have not had, however, the opportunity of observing any positive case that bears conclusively on the cortical localization of peripheral vision. This is not surprising, as penetrating or perforating wounds which could involve directly the anterior portion of the calcarine region are very liable to injure at the same time the optic radiations. It is not uncommon, however, to find the so-called "telescopic vision" in patients who have been shot through the head in the lower parietal or temporal regions, as in the following case:—

Case 23.—Private F., 8,243, was wounded probably in the middle of June, 1915; he was unconscious for some days and was admitted to a base hospital on June 18.

Wound.—The entrance was 2 in. (5 cm.) above and $1\frac{1}{2}$ in. (3·75 cm.) behind the upper margin of the attachment of the right pinna; the exit was $\frac{1}{2}$ in. (1·25 cm.) above and $2\frac{1}{2}$ in. (6·25 cm.) behind the attachment of the left pinna. Both were small, punctured wounds. He was in a very drowsy and critical state when admitted, and had papillœdema with swelling of the discs of about 3D. and small hæmorrhages in their neighbourhood, but he improved rapidly after a decompression operation had been performed. The wounds healed rapidly and the papillœdema disappeared, but his vision was then found to be seriously affected. Six weeks after the infliction of the wound he could only read large letters, and his visual fields were limited to a zone of about 10° around the fixation point (fig. 27). He was able to recognize colours by macular vision. In this case measurements show the bullet probably passed the middle line of the skull, posterior to the splenium

and through the anterior part of the area striata, but as the optic radiations must have been also injured, the interpretation of his visual disturbance is doubtful.

It might, perhaps, still be argued that the evidence is not sufficient to conclude that central vision—that is, that subserved by the fovea

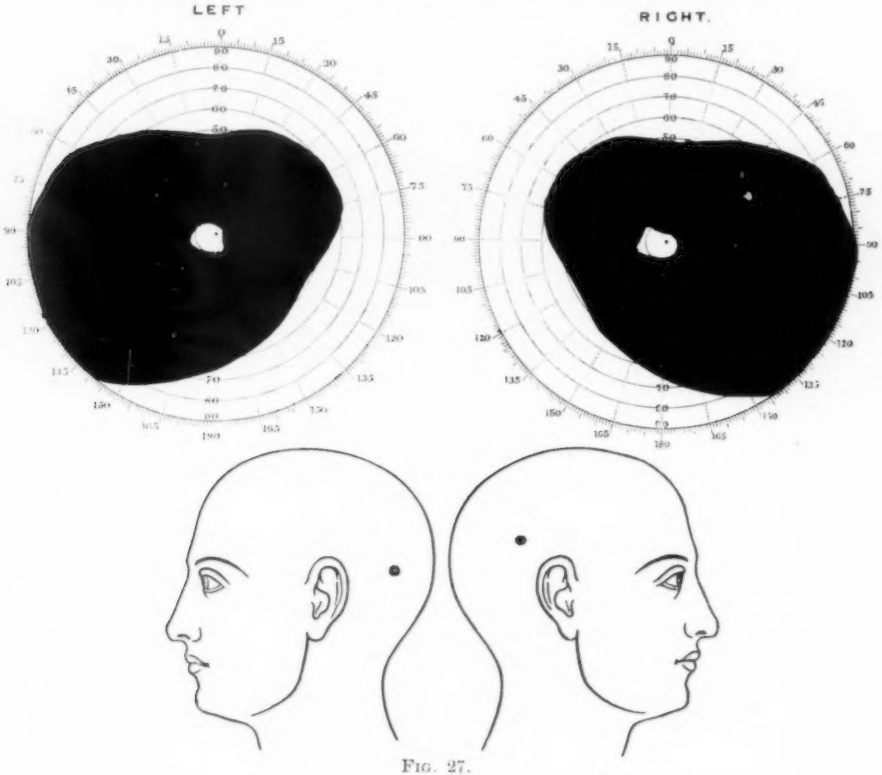

Fig. 27.

centralis—has not a double representation in the cortex, as certain of our fields may show that the blindness, whether in the form of a scotoma or of hemianopia, did not extend up to the fixation point; but we have found that the more exact the methods we employed, and the greater the care taken in making the observations, the nearer did the defect approach the fixation point. We consequently believe that, in common with every other part of the retina, the macula is not represented bilaterally.

In a certain number of the visual fields reproduced the areas of blindness are not quite symmetrical in the two eyes; in dealing with central scotomata this may be due to the obvious difficulty in obtaining central fixation, and in other cases to failure or fatigue of attention on the part of the patients suffering with recent head wounds. This tendency for attention to fail generally necessitates frequent short sittings in order to obtain accurate records.

Another point of interest is whether vision for colours may be dissociated from that for white—if, in other words, an achromatopsia may be produced by cerebral lesions. It is true that in certain cases we found the perception of colour lost in areas in which white was visible, but in such regions of the visual field vision even to white was indistinct and uncertain, especially when small test objects were employed. It consequently seems that loss of colour vision for objects of the ordinary test size (10 mm.) may be only a part of general reduction of visual acuity; we can, however, only state at present that we have no conclusive evidence that achromatopsia, with intact vision for white, is produced by cerebral lesions which involve either the cortex or the optic radiations.

Such observations as those we put forward here will be, no doubt, multiplied during the course of the War, and when finally collected should furnish fuller and more definite conclusions on localization within the cortical visual area. Inouye has attempted this from his observations on men wounded in the Russo-Japanese War, and Dimmer, Uhthoff and Axenfeld have already described a certain number of important cases seen during the present conflict.

While this paper was in preparation the valuable and elaborate contribution of Pierre Marie and Chatelin to the same subject has come into our hands. We need only add that our work seems to be mutually confirmatory.

Our conclusions, which cannot yet be regarded as final, may be formulated concisely:—

(1) The upper half of each retina is represented in the dorsal, and the lower in the ventral part of each visual area.

(2) The centre for macular or central vision lies in the posterior extremities of the visual areas, probably on the margins and the lateral surfaces of the occipital poles.

(3) That portion of each upper quadrant of the retina in the immediate neighbourhood of, and including the adjacent part of, the fovea centralis is represented in the upper and posterior part of the visual area in the hemisphere of the same side, and vice versa.

(4) The centre for vision subserved by the periphery of the retinæ is probably situated in the anterior end of the visual area, and the serial concentric zones of the retina from the macula to the periphery are probably represented in this order from behind forwards in the visual area.

Finally, it is our pleasure to acknowledge gratefully the help and assistance we have received from the medical officers of the various hospitals in which the patients were observed.

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A NEW FAMILIAL, INFANTILE FORM OF DIFFUSE BRAIN-SCLEROSIS.

BY KNUD KRABBE, M.D.COPENHAGEN.

From Queen Louise's Hospital for Sick Children [Professor MONRAD], *and from the Children's Department of the University Hospital, Copenhagen* [Professor BLOCH].

IN a previous paper [12], three years ago, I described a case of a peculiar affection in the brain of a child. This case I regarded as an early stage of the disease named "diffuse sclerosis of the brain," and in consequence of the characteristic histological findings I called this preliminary stage "perivascular necrosis of the medullary substance."

In the case in question the patient was but 1 year old, and it struck me that few cases in earliest infancy were to be found in international literature. Soon afterwards, however, I had an opportunity of seeing such a patient demonstrated, and after the death of the patient I was permitted to perform an autopsy and make a microscopic examination of the central nervous system.

The chief peculiarity of this case was its familial occurrence, which, at any rate from a pathogenetic point of view, rendered it different from all other cases described as infantile diffuse sclerosis. Further examination now showed that besides this case four other similar cases had been observed at the Dronning Louise's Boernehospital (Queen Louise's Hospital for Sick Children) and in the private practice of Professor Bloch—viz., the sister of the above-mentioned patient, two members of another family, and an isolated case. Two of these five patients have been demonstrated by Professor Monrad in the Pediatric Society of Copenhagen. Specimens from one of them, moreover, were demonstrated by Dr. V. Poulsen in the Section for Morbid Anatomy of the Biological Society. The third case had been briefly mentioned in the Pediatric Society by Dr. Joergen Bech and Dr. Monrad, and the two last cases during a discussion in the Pediatric Society by Dr. Bloch.

A thorough comparative and detailed report of these cases does not, however, exist, and the present paper may therefore be of some interest.

In the following paper infantile sclerosis of the brain alone will be

discussed, as, according to my view, the disease in children is somewhat different from that in adults.

I have much pleasure in recording my indebtedness to Professor Bloch and Professor Monrad for kindly permitting me to publish these cases. I am also indebted to Dr. V. Poulsen, who meant to publish the clinical history of two of the cases, but kindly left them at my disposal. Furthermore, I wish to thank Dr. K. Malling, who had prepared specimens from one of the patients, but generously handed the case over to me; and Professor Friedenreich, who permitted me to work out one of the cases at the Psychiatrical Laboratory of the University (the main part of my investigation was carried out at the laboratory of the Children's Department of Rigshospitalet).

Case 1.—Kai Bn., son of a confidential clerk, born on November 25, 1912, died at thirteen months old. He was the second of a family of two: an elder sister suffered from the same disease, and is described below (Case 2). The father in his youth is said to have had hæmoptysis, the mother had always been healthy. Syphilis was denied. The patient was born normally at full time, the weight being at birth $3\frac{3}{4}$ kg. Up to the age of five months he developed fairly normally, was quick and gay, able to move his limbs freely. During the first four months he was suckled, but after that time was given milk-soup with bread and milk. When five months old he began to cry frequently and convulsively. At the same time fits of stiffness of all extremities appeared, with obstetrical posture of the hands and crossing of the legs. In the intervals between the attacks the patient was very weak and not able to sit up. The temperature was occasionally 38·2 C. in the afternoon, but generally normal. The stools were mostly normal, and, except during the first months, there was neither regurgitation nor vomiting.

On July 7, 1913, the patient was admitted to the Queen Louise's Hospital for Sick Children, where physical examination gave the following result: Weight, 7,050 grm.; length, $62\frac{1}{2}$ cm.; circumference of the head, $43\frac{1}{2}$ cm.; circumference of the chest, 42 cm.; greatest circumference of the abdomen, 37 cm.; fontanelle, 3 cm. by 3 cm., normal tension; teeth, 0; temperature, 37·3 C.; urine acid, turbid with urates, no pus nor albumen. The child was well nourished, sunburnt, normal appearance. Pupils large and active to light. No nystagmus. External examination of the eyes, ears and fauces showed no abnormalities; ophthalmoscopic examination showed greyish discs with veiled outlines (early optic atrophy). The patient followed things with his eyes. Slight universal micro-adenitis Stethoscopic examination and examination of the abdomen showed no abnormality. No signs of rickets. Intense sweating. Violent crying and gasping during the examination. Body and limbs stiffly extended, head turned backwards, back crooked, hands often clenched, sometimes in tetanic posture; lower extremities strongly extended and adducted, toes spread (figs. 1 and 2). The examination of reflexes was difficult,

but Babinski's sign was present. During the examination attacks of convulsion occurred, which made the lower extremities still more stiff, head and back were drawn more backwards, arms moved up and down in clonic spasms. The fits were accompanied by convulsive crying and gasping. The attacks appeared without any obvious cause.

The course of the illness during the six months' residence was as follows: The Wassermann test on July 13 was negative; v. Pirquet negative. Lumbar puncture on November 10 showed about 3 c.cm. slightly turbid fluid, containing

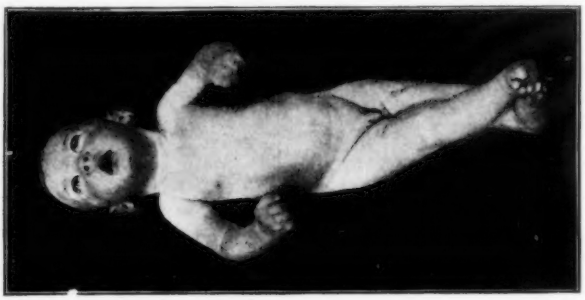

FIG. 1.—Case 1, Kai Bn.

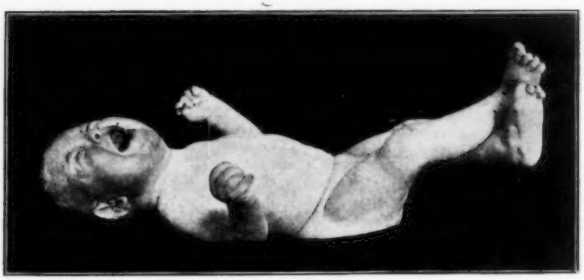

FIG. 2.—Case 1, Kai Bn.

a few endothelial cells but no other cells and no micro-organisms; there was no growth on agar, serum, bouillon, or ascites agar. The stools were nearly always normal even during the febrile periods. From July 23 to July 28 only were they found to contain some mucus, and on November 28 (during a period of fever) they were watery. There were, as a rule, one to three stools a day. Regurgitation occurred now and then, but no vomiting. The urine never contained sugar nor albumen, whereas on November 6 and the ensuing days

some pus was observed. When examined under the microscope (November 13) the urine was found to contain numerous leucocytes, a number of epithelial cells, and *Bacillu coli*, but no cylindrical cells or red blood corpuscles. The weight (on admission 7,050 grm.) increased during the first days some 100 grm., after which, during the following days, it dropped down to 6,300 grm. It then oscillated periodically between 6,200 and 6,800 grm., until it fell rather abruptly to 5,700 grm. The loss of weight, as a rule, appeared coincident with the febrile periods. The patient was fed at first on milk-soup and water (equal mixture), then pure milk-soup.

August 1: Patient sometimes dull, sometimes crying, falls into spasms at the faintest noise. Sleeps well at night; bathing appears to have a calming effect. He is able to follow movements with his eyes. No nystagmus. The stiffness of body and limbs unchanged.

August 25: Has gained in weight. Has been somewhat more quiet during the last days, but lies constantly in a spastic state; frequent exacerbations occur, in which his hands are clenched violently, arms moved to and fro, head drawn backward, and back crooked in arc de cercle, lower extremities extended, a slight indication of tetanic posture of the feet, no real nystagmus. The fits seem to cause pain, and are hardly followed by unconsciousness. In the upper extremities the reflexes are easily obtained, but ankle-jerks were not brisk. The knee-jerks were not obtained. Plantar reflexes normal.

December 1: Condition has grown worse, more difficulty in swallowing, and increased dulness.

December 29: Some cyanosis of the face since yesterday. No convulsions. Died at 12.30 p.m.

Dr. V. Poulsen, who saw the patient daily, characterized the case in the following way: An intense stiffness of all the extremities was observed during nearly all the time of residence in hospital. When examined, or when loud speaking took place in the room, he at once fell into tonic spasms. The dulness, however, did not appear until the last days, when he grew more debilitated, and the spasms were then excited only by stronger irritation. At the same time the eclamptic fits began, during which universal clonic and tonic convulsions appeared, combined with marked cyanosis.

It may be added that the elevations of temperature, before mentioned, were never followed by cough, dyspnœa, or other signs of pneumonia.

The clinical diagnosis was: sclerosis cerebri diffusa.

Post-mortem examination ten hours after death gave the following result: The body was that of a moderately nourished child; *rigor mortis* present. In both lungs extensive red, infiltrated, partly confluent portions of a typical pneumonic appearance. The mucous membrane of the bronchi hyperæmic. No signs of tuberculosis. Heart, stomach, intestines, liver, kidneys, spleen, pancreas, thyroid gland, and suprarenal bodies showed no abnormality. On opening the skull, theca and dura were found to be normal. From the subdural and subarachnoidal cavities a considerable amount of clear cerebrospinal fluid was evacuated. The brain occupied less room in the thecal cavity than is the

case with normal brains; its weight was 650 grm. Pia œdematous, not thickened nor of milky consistence. The ventricles of the brain were not distinctly dilated; no granulation of the ependyma. The consistence of the brain, cerebellum and spinal cord was found to be increased, so that the brain did not show any tendency to flow out after removal, as is generally the case with children's brains of that age, but kept its form, with medulla oblongata protruding into the air. The increase of consistence was most pronounced in the cerebellum and medulla. On the cut surface the cortex appeared to be soft without any abnormality, the medullary substance was harder and, especially in the most central parts, greyish-red, but whitish in the thin subcortical layers.

Blocks were immediately taken for microscopical examination, hardened in 96 per cent. alcohol, Müller's fluid, Weigert's stain for neuroglia, and 10 per cent. formaldehyde respectively. Some of the pieces hardened in formaldehyde were later on prepared in Flemming's fluid. The rest of the brain was kept in 4 per cent. formaldehyde and after some months large slices (transverse sections) were transferred into Weigert's brown chromic acid stain. The following methods of staining were carried out: Nissl's thionin staining, Weigert-Kulschitzsky-Wolters method, and Spielmeyer's method of staining for medullary sheaths, Marchi's staining, Bielschowsky's staining, staining of the fat with Sudan red, Alzheimer's method of staining for neuroglia with Mallory's hematoxylin, and Alzheimer's acid-fuchsin—vert-lumière staining. The last method especially gave fine glia pictures. As in my previous work on sclerosis of the brain, I have here embedded in paraffin at low temperatures.

Microscopic examination gave the following result:—

The hemispheres of the cerebrum.—The pictures of the medullary sheaths (stained by Weigert-Pal) show to the naked eye an enormous destruction, so that the white matter is found to be almost as pale as the cortex (fig. 3). Immediately under the cortex only a narrow streak (1 cm. to 2 cm. in width) of darker stained tissue is visible. Under the microscope, however, the destruction appears to be not quite total: a scanty number of medullated nerve-fibres are found crossing in all directions. The destruction of the medullary sheaths in the white matter is not quite evenly distributed, and a thin layer of much less destroyed tissue is found in the peripheral regions. In addition, the central part of the white matter contains small scattered islets of totally destroyed tissue, while the surrounding plexus is relatively less destroyed. On the whole, the destruction increases towards the centre. The areas around the smallest vessels are, as a rule, not specially affected by the destruction, while the bigger ones are surrounded by a thick border of totally destroyed sheaths. In the cortex, on the other hand, slight wasting only of the medullated fibres is traceable; both tangential

fibres and supra- and inter-radial fibres are present, although somewhat more scanty than usual.

In large sections (fig. 3) of the brain stained by the method of Kulschitzsky-Wolters and Pal the process was found to be uniform throughout the whole cerebrum, and no normal white matter was left except the thin subcortical layer, which was everywhere preserved. In Marchi specimens only a very small number of blackened granules are found in the white matter and in the cortical substance. In the big cells which surround the vessels and fill up the vessel sheaths only small collections of cells are occasionally observed, the granules of which are blackened with the osmic acid.

FIG. 3.—Section from the occipital lobe of the brain of Case 1, Kai Bn. Staining of Weigert-Pal. The black line between the cortex and the medullary substance represents the only remains of the white substance, the lighter part inside this line is medullary substance, who is replaced by neuroglia and therefore uncoloured.

Bielschowsky specimens show an immense destruction of the axis cylinders corresponding with that of the medullary sheaths, so that only a small number are found to radiate widely, and even these are to some extent in granular decay. In the cortex, however, the nerve-cell processes seem to be quite as numerous as in a normal brain, although some of them are in granular decay and irregularly thickened, possibly due to *post-mortem* changes. Cajal's corpuscles cannot be observed.

The specimens stained for neuroglial changes clearly illustrate the positive corresponding with the negative findings of the medullary sheaths. In specimens stained with acid-fuchsin—vert-lumière (figs. 12 and 13, pp. 104, 105) a red substance is visible to the naked eye, corresponding with the white matter. When examined under the microscope this substance is found to consist of glia-fibres, the number and density of which are fairly uniform throughout the whole field of view. In a thin layer surrounding some of the largest vessels, the glia-fibres, however,

seem most closely packed together, taking here the same longitudinal direction as the vessels. Among the glia-fibres cells of very different shape and size are traceable. Some of them are small and mononuclear, containing but a very thin protoplasmic layer. In other cells the protoplasm is of almost gigantic dimensions, forming a roundish or irregular outline, sometimes homogeneous, sometimes slightly granular, with big vacuoles or recesses. Between these cells and the smaller ones transitional forms are found, mostly irregular or lobed in outline. The contents of chromatin of the nuclei varies greatly: the bigger the cell, the more scanty the chromatin. The nuclei generally contain one or two nucleoli, and as a rule are arranged excentrically. It is not, however, evident from these glia pictures whether or not the cells are sending out processes, while in specimens stained by Alzheimer-Mallory's method (fig. 16, p. 107) cell processes enclosing the glia-fibres are distinctly visible. On the other hand, the typical amœbic glia-cells are here extraordinarily few in number. The distribution of cells is fairly uniform throughout the glia substance; in the outer subcortical layer perhaps the number may be somewhat smaller than in the central regions round the vessels, where the bigger glia-cells are replaced by cells which fill up the adventitia sheaths of the blood-vessels (fig. 13). A great number of these cells have a large round protoplasm, similar to that of the bigger glia-cells: they are, however, more degenerated and contain pale homogeneous nuclei and nucleoli which have entered the protoplasm, and finally oblong cells which seem to fit into the shape of the vessel sheaths. Granules stained by osmic acid are, however, of very rare occurrence in these cells. On comparing these specimens with those stained with Sudan red only a very small number of them will be found to contain fatty granules. This is quite in keeping with the pictures of the medullary sheaths, where only very few bluish-black granules are found in the cells. It may be added that the vessel sheaths only contain these "empty fatty granule-cells" and "scavenger cells" (Alzheimer's Abräumzellen), and nowhere any sort of inflammatory cells —in fact, neither plasma-cells lymphocytes, nor polymorphonuclear leucocytes.

In the cortex the condition is quite different to that of the white matter. The outer glia is hardly thickened, and only occasionally in the cortex itself a single thread-forming glia-cell (*see* fig. 14, p. 105) may be observed. The vessel sheaths nowhere contain scavenger or other cells. The boundary between cortex and the white matter stands out rather distinctly in the glia pictures macroscopically. On microscopic examina-

tion, however, a transitional region is observed in which the number of glia-fibres and cells is seen to decrease towards the cortex. This region apparently corresponds with the thin layer of preserved medullary sheaths. In specimens stained by Nissl's method, protoplasmic glia is found corresponding with the white matter, and scavenger cells similar to those mentioned above. More distinctly than in the real glia pictures, these specimens present small, intensely stained corpuscles resembling the calcareous concretions of the meninges and pineal gland arranged round the blood-vessels. The nerve-cells of the cortex apparently show no abnormality; the condition of the Nissl granules cannot be made out definitely, as the *post-mortem* examination was not carried out till ten hours after death; at any rate, no important Nissl changes can be seen. The appearance of the nuclei is normal, there is no pycnoid change of the protoplasm, and no abnormal number of big cells. On the whole, no destruction of the nerve-cells can be seen.

In some places the pia appears to be somewhat thickened and rich in cells, but is nowhere infiltrated. The vessels of the cortex are normal, whereas those of the white matter at the first glance look pathologically changed. When examined more closely, the intima and media, however, appear to be normal, and the changed appearance of adventitia is due to the great number of scavenger cells.

The mid-brain shows on the whole the same changes. The destruction of the medullary sheaths, however, does not seem quite as extreme as that of the hemispheres, and apparently diminishes towards the pons. Marchi degeneration cannot be seen, and fatty granules are only rarely visible. The destruction of the axis-cylinders of the white matter seem to be parallel with that of the sheaths. The nerve-cells of the great ganglionic centres present a similar appearance to those of the cortex. In the nuclei of the cranial nerves the Nissl pictures show unchanged nerve-cells; distinct Nissl granules are seen, and there are no acute changes. A glial increase is seen in the mid-brain similar to that of the hemispheres, although somewhat less sharply limited, and similar glia-cells and scavenger cells are traceable. Furthermore, pathological changes are seen similar to those found in gliomata (*see* fig. 15, p. 106), gigantic cells with a large, irregularly outlined protoplasm and several nuclei placed peripherally or embedded in niches. In addition to these, a number of smaller cells with degenerated nuclei and thick protoplasmic processes are found. Among these cells a multitude of processes are seen crossing each other obliquely, or in some places showing a parallel course. Among these thicker fibres, ordinary thin glia-fibres

are noted, and finally in addition transitional stages. The giant-cells, which at the first glance had some resemblance to degenerated nerve-cells, are pathological forms of glia-cells if anything, as some of the processes are found to contain glia-fibres.

Cerebellum.—In specimens showing the medullary sheaths a still greater destruction is to be seen, which does not decrease in the most peripheral part of the white matter. In the grey matter also destructive processes are observed, proportionately less marked in the stratum granulosum. Marchi degeneration is nowhere traceable. The axis-cylinders are somewhat better preserved than the myelin sheaths. In the glia specimens the white matter is seen to be replaced by dense fibrillar glia, containing both big and small glia-cells. The increase of glia, however, is not only found in the white matter, but also in the granular layer, and even in the molecular layer, where some isolated glia-fibres passing radially are seen. The vessel sheaths contain scavenger cells, in some places filled with fatty granules. The stratum granulosum does not show anything particular in the Nissl specimens, whereas Purkinje's cells appear to be somewhat shrunk and seem to have somewhat defect processes.

Bulbus olfactorius was examined by Nissl's method only; no prominent changes of the cells nor infiltration of the vessel wall can be observed.

In the *tractus opticus* and *chiasma* an intense destruction of the medullary sheaths is seen, especially perivascular, around the vessels; rarely the denser bundles are preserved. Except in some places around the vessels the axis-cylinders have also been destroyed for the most part, corresponding with the regions where the medullary sheaths are totally destroyed. Corresponding with the destruction of the myelin sheaths, an immense number of glia-fibres and cells are seen, showing the same appearance as those of the hemispheres. In the adventitial sheaths of the vessels and round the vessels, scavenger cells and fatty granule-cells are of very rare occurrence.

The spinal cord and medulla oblongata.—Throughout all the sections of the spinal cord a diffuse destruction of the medullary sheaths is to be found in the white matter. It is most advanced in the pyramidal tracts, which at this period of life ought to be developed and least pronounced in the root entrance zones. In the grey matter no signs of destruction can be seen. The Marchi degeneration is just as scanty as was the case in the cerebrum. The destruction of the axis-cylinders seems less pronounced than that of the sheaths. In the pyramidal

tracts, however, very few axis-cylinders are present. The grey matter shows a fine figuration of axis-cylinders and of the intercellular fibrillæ. Corresponding with the destruction of the medullary sheaths a very conspicuous proliferation of the glia is observed. In the outer parts are seen strong radial projections, among which lie a scanty number of fibres, crossing into all directions. Among the glia-fibres cells are observed of very varying appearance, as was the case in the brain. The glia has no particular relation to the vessels. The adventitial sheaths are usually filled with big scavenger cells, which in specimens stained with Sudan red appear to contain no fatty granules at all.

In the grey matter no glia increase is found, and there is no abnormality in the tissue surrounding the central canal. Here, too, the nerve-cells appear to be preserved and the Nissl's figures and neurofibrillæ are clearly defined and normal.

Case 2.—Bodil Bn., daughter of a clerk, was born on February 21, 1911; died at the age of 1 year. The patient, the elder sister of the first patient, was born normally at full term. The weight at birth was 4 kg. It was noticed by the midwife that the child was unusually stiff, and immediately after birth rigidity of the nape of the neck was discovered. Up to the age of four months she was suckled; then she was given barley broth, milk, water-gruel, Nestlé's food, and unboiled milk. The patient, however, after weaning had fits of crying and frequent vomiting, which abated as soon as the patient was put upon buttermilk. She was often slightly febrile for a few days in succession. Development proceeded normally until the fourth month, after which she did not advance mentally and was hardly able to recognize her mother. The stiffness of the neck and legs continued, and the fits of crying were spasmodic, accompanied by severe congestion, but regular convulsions did not occur.

On November 7 she was admitted to the Dronning Louise's Boernehospital (Queen Louise's Hospital for Sick Children), and physical examination there showed: weight of body, 4,700 grm.; length of body, 64 cm.; circumference of head 40½ cm.; circumference of the chest, 39 cm.; greatest circumference of the abdomen, 31 cm. The expression was rather stupid and vague, the cry hoarse and convulsive. The pupils were active to light. The child was lying stiffly bent backwards, with marked opisthotonos and strong lordosis of the lumbar region. Universal rigidity of the muscles was most pronounced in the lower extremities, which were hyperextended and adducted. Hands and feet were in the tetanic posture. The appearance of skull and eyes normal. Ophthalmoscopic examination (September 9) showed the right disc white and atrophic, the left pale. Fauces normal; stethoscopic examination normal; abdomen somewhat contracted (figs. 4 and 5).

The patient seemed conscious and sensitive to pain. Examination ten days later showed almost continuous tonic rigidity of all muscle groups

combined with the tetanic posture. Now and then periods of violent spasm appeared, especially in the lower extremities and in the back and neck, so that "arc en cercle" appeared. Nystagmus was sometimes present. The pupils reacted rather slowly to light. She never smiled, never seemed to be conscious. The fontanelles were large and sunken. The plantar reflexes brisk, but of uncertain form. The patellar reflexes could not be obtained on account of the rigidity.

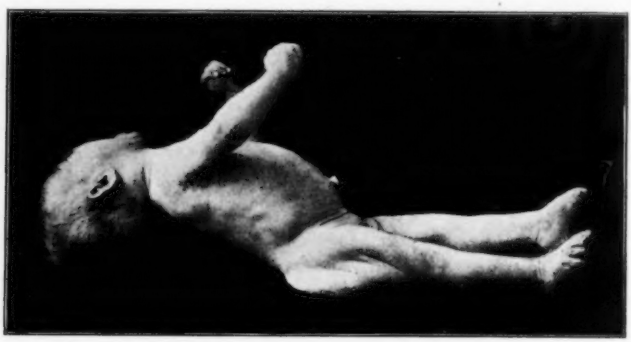

FIG. 4.—Case 2, Bodil Bn., aged 7 months.

FIG. 5.—Case 2, Bodil Bn., aged 7 months.

Examination of the organs showed nothing abnormal. No rickets. Wassermann's test (October 19) negative; v. Pirquet (September 17 and October 10) negative.

As to the course of the illness, the following facts were stated: The temperature was normal at first; after a fortnight slight elevations (to 38° C.) were noted during the following week. Then again a week passed with normal temperature, succeeded by a febrile period.

Up to October 27 the temperature remained raised, but then became normal again after a week. Then it ran an irregular course ranging between normal

and 38° C.; for a few days a subnormal temperature was noted, then again a normal and slightly raised temperature alternately. For about a fortnight from December 21 the temperature remained normal or subnormal, and then after a short febrile period began to oscillate between 34° C. and 38·3° C.

The stools were normal throughout, except on one day. In the beginning there was frequent vomiting, which later occurred once or twice a day. In the last month vomiting did not occur at all. The urine contained traces of albumin and epithelial cells, urates, a number of cylinders, but no leucocytes. No growth occurred. On later examinations it did not contain albumin. The weight on admission was 4,700 grm., was steadily increased during the following months up to 5,600 grm., then decreased during the next month, until at last it fell rather abruptly to 4,800 grm.

The patient was given buttermilk for the first two days, and after this milk and barley water in equal parts seven times a day; this was increased to pure milk 150 grm. seven times a day.

Her progress was as follows :—

October 18: Patient drinks well; good stools; has gained in weight; condition all but unchanged, more or less spasmodic, sometimes interrupted by violent tonic spasms, which are nearly always accompanied by screaming. These attacks are evidently very painful, and are roused by the faintest influence from without, as, for instance, by sudden light or touch. More marked nystagmus than before. Corneal reflexes scarcely obtained, the pupils are but slightly active to light. Circumference of head, 42 cm.; circumference of chest, 39½ cm. The fontanelle: 3 cm. by 3½ cm., distended only during the attacks. Regurgitation and vomiting are frequently reported. Action of the heart regular.

October 28: Drinks poorly, condition much worse since the last note, scarcely any reaction to noise, attacks produced only when she is touched. Vomiting again of frequent occurrence.

January 13: Previous fits of crying all but ceased; very insignificant spasmodic stiffness. Plantar reflexes still rather brisk, most of the other reflexes abolished. Nystagmus rarely observed. During the last few days difficulty in swallowing has supervened.

February 6: Patient is lying unconscious, not able to swallow. Died at 8 a.m.

Post-mortem examination, nine hours after death (Dr. Oerum), gave the following results: Small scattered, apparently hypostatic, pneumonic patches, but no other special abnormality; no signs whatever of lues.

The most conspicuous pathological changes were found in the central nervous system, examined by Dr. Malling, who has given the following description: The brain and the spinal cord, in contradistinction to the soft, nearly confluent central nervous system generally found in children, is solid and hard and keeps its shape. There is no difference as to hardness between different regions; the sclerosis is diffuse and affects the cerebellum and the mid-brain. The gyri throughout the brain stand out distinctly and are

unusually small and slender. The nerves of the base, especially the optic nerves, are solid, hard, and thickened. The pia is somewhat thickened and indistinct. The cortex is of normal colour and depth, and immediately under it a streak of normal white medullary substance (2 mm. in width) is seen, but more centrally the white matter presents a peculiar greyish translucent colour, the knife passes easily through the cortex, whereas the rest of the substance of the brain is tough and hard to cut.

Sections were made from the frontal and occipital lobe, from the gyrus paracentralis, from the cerebellum, and from the dorsal, cervical and lumbar regions of the spinal cord, the optic and facial nerves. The following methods of staining were pursued: The ganglion cells were stained with thionin (method of Nissl), van Gieson, Weigert's staining for elastine and for neuroglia, Kultschitzsky-Wolters' staining for medullated nerves, Marchi staining and Bielschowsky's method of staining for neuro-fibrils, various methods of staining glia (Alzheimer), Levaditi's silver method of staining spirochætes.

Dr. Malling's description of the microscopical examination is as follows. To this, after having re-examined the specimens, I have added some supplementary notes in parentheses.

Cerebrum.—Pia appears to be somewhat thickened, especially above the motor region, but no great infiltration of cells is traceable. Most of the cells are fibroblasts and fatty granule-like cells. No plasma cells. (The thickening seems to be due essentially to œdema.) On examining under low magnifying powers specimens of the brain stained with thionin, the cortex is found to be, on the whole, fairly well preserved; it contains the usual layers of cells, but in the motor region the giant pyramidal cells are diminished. Just inside the cortex a light zone is seen, visible also to the naked eye, which contains a few cells only; more centrally, the whole white substance stains intensely, the colour increasing towards the centre. The most prominent feature of this zone is a multitude of blood-vessels, surrounded by large intensely stained cells, and it is clear that the main incidence of the process falls upon the vessels. Under high magnifying powers a chronic inflammation of the ganglion cells is seen, the nuclei are diffusely stained blue, the protoplasm is in granular destruction, otherwise the cortex appears to be quite normal. There is no noteworthy increase of the glia, nor any new formation of the vessels. No cells of infiltration. In the more highly stained zone, just internal to the cortex, no abnormality of the vessels can be seen; as a rule polynuclear glia-cells are visible. Still more centrally in the white matter a confusion of various cell forms appears. On examining a typical blood-vessel the lumen is not particularly diminished, and is as a rule empty; then comes the endothelial

layer with nearly normal cells and without any special proliferation; then, in most cases, a more or less light zone. But as soon as we reach the adventitia and perivascular region an enormous proliferation of large epithelial cells is observed, felted together and more or less angular, in contradistinction to the round cells of the tissue. These cells often contain a number of nuclei, peripherally arranged and always degenerated. The protoplasm is stained diffusely, and, in some of the cells, large dark clumps, like degenerated nuclei, are found. The said cells are placed in one or several layers round the vessel. The tissue contains similar cells, the dimensions of which are often gigantic, but they seem here more prone to vacuolar degeneration; sometimes they contain several small, sometimes one big vacuole, and thus perhaps are transitional stages to the real fatty granule (basket?) cells. The latter are found in great numbers in the tissue or in some of the vessel sheaths, as may be seen from the Marchi specimens (black-stained lipoid grains). The large cells mentioned above do not contain lipoids. In addition to these cell forms, a number of small dark nuclei with a scanty and somewhat tattered protoplasm are noticed in the glia-cells. Some of the vessels are apparently normal. The above changes are also present in the frontal, occipital and paracentral gyri.

In specimens stained for medullated nerves, scanty remnants only of the sheaths are traceable. The tangential and supra-radial fibres appear to have been completely destroyed, possibly owing to a too strong differentiation, and in the central part of the white matter there are practically no fibres; whereas, corresponding to the above "light zone," immediately under the cortex some fibres are seen, although they are considerably degenerated.

So much for the frontal and paracentral gyri. In the occipital gyri more fibres are found, and the zone of Baillarger is extraordinarily well preserved. As a sort of compensation for this almost complete destruction of nervous substance in the white matter, specimens stained for neuroglia by Weigert's method show an enormous proliferation of the glia to a degree that cannot be equalled in any other affection of the brain. The number of glia-nuclei is rather small in proportion to the glia-fibres. The fibres are, as a rule, thin and slender. In contradistinction to this enormous subcortical gliosis no increase worth mentioning is found in the cortex or marginal glia.

Similar changes are observed in the cerebellum. In the central part of the white matter the cells and changes are exactly the same as in the cerebrum; they decrease towards the granule layer, which is less

compact than usual and swarms with a number of cells, evidently glia-cells. The cells of Purkinje are somewhat degenerated and the medullary sheaths are totally destroyed, but for some few traces in the granule layer. Small bundles of medullary sheaths are also found to be intact in the white matter. In specimens stained by Bielschowsky's method, it is seen that the axis-cylinders are also destroyed. In the cerebellum also the degenerated nerve tissue has been replaced by glia, which stretches into the granule layer and runs as fairly parallel fibres right through the molecular layer to the surface (Bergmann's fibres).

The optic nerve and, to some extent, the facial nerve show more or less complete destruction, the former being transformed into glia tissue.

The cervical spinal cord, when examined in thionin specimens, appears to be somewhat effaced, so that the line of demarcation between the grey and the white matter is not easy to make out. In the grey matter large portions, especially the anterior horn-cells, are destroyed. This, however, is in our opinion somewhat doubtful, as the large motor cells of the anterior horn are also extraordinarily well preserved. All through the grey and white matter a conspicuous new formation of blood-vessels is observed, and cells similar to those of the brain, with vacuolation and a multitude of glia-cells, are present. In specimens stained for medullated nerves the whole transverse section of the spinal cord appears to be greatly degenerated, although not quite uniformly; the grey commissure, the spinal cerebellar tracts and the root-zones are the best-preserved portions, the anterior and Burdach's columns are moderately degenerated, and Goll's columns and the pyramidal tracts are completely destroyed. The fibres of the grey matter are much degenerated. In glia specimens the enormous marginal gliosis sending out thick glial septa into the substance is the most dominant feature; for the rest, the glia tissue is strongly increased throughout the transverse section.

Changes similar to these are found in the dorsal and lumbar cord. In the dorsal region the degeneration of the medullary sheaths is found somewhat more centrally in the posterior column, whereas in the latter place moderately preserved spinal cerebellar columns are not observed. In the cervical and less distinctly in the lumbar cord, in front of the central canal, a rather deep lateral fissure and several smaller fissures are noted.

Weigert's elastic tissue stain does not show any pathological changes in cerebrum, cerebellum, or in spinal cord.

Levaditi's silver method for staining spirochætes gave a negative result.

On the whole, stained specimens from this patient present much the same pictures as those of Case 1, the essential difference being, in my opinion, that the scavenger cells of the vessel sheaths in Case 2 are found to contain far more fatty substances than those of the previous case. It may be remarked that no inflammatory processes were found in these specimens, any more than in those from Case 1.

Case 3.—Agnes A. B., daughter of a bricklayer, born October 10, 1904, died in the Dronning Louise's Boernehospital (Queen Louise's Children's Hospital) at the age of nine months.

The patient was the eldest child; her younger sister is described as Case 4. She had a convergent squint from birth. She was brought up on the breast and thrived well, except for the stools, which were green; this caused the mother to apply to the polyclinic of the hospital. The meals were regulated, bismuth was given, but the stools remained unchanged. At the age of five months attacks of diarrhœa occurred, and a week later stiffness of the body with opisthotonos and violent screaming. Patient took fluid food poorly, vomiting being rather frequent.

On April 5, 1905, she was admitted to the hospital and physical examination showed: weight, 4,358 grm.; temperature, 37·5° C. She was a slender, well-nourished child. Stethoscopic examination normal; ears and fauces normal; a small umbilical hernia was noted; the fontanelle was not distended, but if anything somewhat sunken. Strabismus convergens present. No facialis or Trousseau's symptoms. During examination there were frequent attacks of total stiffness of the body and extremities, followed by opisthotonos; the arms were flexed at the elbow-joint, fists clenched with the thumb partly within, partly outside the other fingers. The lower extremities were extended and the feet in plantar flexion. Nystagmus of both eyes; patient yawned often and violently, smacking her lips now and then; colour did not change. The stools at first were thin, greenish, acid, aromatic-smelling, then mucous with an alkaline reaction. When examined under the microscope they were found to contain only mucus and a few decaying cells (epithelial and pus). The stools remained thin and mucous; on repeated examination (February 15) a few fatty acid crystals and mucus with a few cells were noted. During the whole residence in the hospital the stools remained mucous and thin in spite of change of diet. Vomiting was of almost daily occurrence and regurgitation very frequent.

The weight on admission, 4,350 grm., in the following fortnight was increased to 4,600 grm., after which it dropped down to 3,400 grm. During the last time again it rose to 3,900 grm. Lumbar puncture gave a negative result. The urine passed was scanty on April 9, 10, 11, but later became abundant, and on April 9 was slightly turbid, contained a slight amount

of albumen and no sugar. On ensuing examinations albumen was sometimes found, sometimes not. The fontanelle remained retracted during the whole stay in hospital. The patient was given the breast once or twice a day, and besides that barley water without admixture at first, then with milk, later on buttermilk soup, children's food, Liebig's soup. Her progress was as follows: —

April 10: Stiffness not diminished; this morning transitory clonic spasms of the lower extremities. More willing to take her food, has sometimes taken fluids well. Somewhat more lively. In the left half of the mouth a considerable reddening of the mucous membrane is found, and on the left side of the palate in the sulcus alveolo-lingualis yellowish mucous projects, which can be removed without difficulty.

April 16: During the last twenty-four hours some convulsive attacks. The patient is rather cold.

April 17: Drinks well. No convulsions, no stiffness of arms and legs. The nape of the neck is now and then drawn backwards, but the spinal column is not stiff. The mucous membrane of mouth and throat clean, red, moist; the palate wound is healing up.

April 19: Again frequent crying. Spastic rigidity of body and extremities. The patient looks very pale. The mucous membrane of the mouth dry, red; here and there ulcerated. Skin elastic.

April 23: Spastic stiffness, slight convulsive spasms of the lower extremities. Condition on the whole unchanged.

April 25: Œdema of hands, feet and thighs.

April 29: Yesterday afternoon one attack of clonic convulsions in the arms and tonic stiffness of legs and spinal column. The nape of the neck bent backwards. Consciousness preserved, no crying, sweating, or congestion during the fits. Occasional nystagmus has been noted. The lower extremities stiffly extended, nearly hyper-extended in the knee-joints. Arms stiffly flexed. Spine not rigid. Œdema of the back of the hand. In the lower extremities scarcely any œdema.

May 7: Dozing; cries only when touched. The lower extremities stiffly extended. In the bath this morning opisthotonos was noted for a moment. No clonic convulsions or laryngeal spasms. Hands cold, otherwise warm. Abdomen somewhat extended in the epigastrium, else otherwise soft; no visible peristalsis, the stomach cannot be marked out.

May 13: Permanent rigidity of legs and spinal column. Heart sounds faint and low.

May 23: Is lying quietly, only wails when touched; is still able to take the bottle; keeps fairly warm. Abdomen intensely sunken. Opisthotonos in the bath, not otherwise. The lower extremities stiffly extended. Some squinting. Scanty secretion from conjunctivæ. Dorsal kyphosis and lumbar lordosis more pronounced than before. In heart and lungs no abnormality. Perpetual yawning.

May 27: Extreme emaciation. Lower extremities constantly stiffly

extended, arms stiffly flexed, nape of the neck bent backwards. Abdomen flattened in the lower part. Epigastrium sunken. On examination the lungs are normal. Heart sounds strong and normal. No hæmorrhages anywhere. No conjunctivitis.

June 6: Œdema of both hands.

June 7: No thrush during the last days. Slight œdema of the upper part of the foot and of thighs. Lower extremities stiffly extended at the hip- and knee-joint. The legs are kept parallel, tightly pressed against one another, and cannot be abducted nor bent passively. Sometimes they are crossed at the ankles. The ankle-joints are slightly plantar-flexed, and the toes, especially the big toe, strongly flexed. The arms are kept at a distance from the body, slightly bent in the elbow, pronated, with the hands dorsally flexed and the fingers tightly clenched into the fist. The thumb is placed at the side of the other fingers. The rigidity of the arm muscles, however, is not so completely wooden as that of the legs. The degree of flexion varies. The spinal column has throughout been intensely arched: a dorsal kyphosis with a corresponding lumbar lordosis. The nape of the neck is stiff and the head is bent backwards, sometimes slightly, sometimes more considerably. The fontanelle is somewhat retracted. Now and then convergent strabismus is present. Some nystagmus. The pupils are equal, of moderate size and active. Perpetual intense yawning, which causes a subluxation of the jaw-joint. No clonic convulsions, no laryngeal spasms. No affection of the face. Abdomen formerly contracted, now rather tympanitic and distended. Taches cérébrales only just traceable. In spite of the evident emaciation she had gained 500 grm. in weight during the last ten days. Pulse not palpable. Heart sounds scarcely audible. Suggillations in the abdominal wall. Ophthalmoscopic examination normal. Left pupil bigger than right.

June 8: Difficulty in swallowing. Discharge of urine ceased. Rigidity as before, spasms did not occur. Died quietly at 8.30 a.m.

Post-mortem examination six hours after death gave the following results:—

An abundance of clear serous fluid was found in the subcutaneous tissue and in all serous cavities. The posterior parts of both lungs, especially the upper lobes, were infiltrated and collapsed. The bronchial and mesenteric glands not swollen. The mucous membrane of the digestive tube seemed normal; no hæmorrhages or swelling of Peyer's patches or of the follicles, which were not even visible. Œsophagus coated with a thick layer of thrush. No thrush in stomach or mouth. Heart, liver, spleen and kidneys were small and normal. The epiphyseal lines of the ribs normal. Spinal cord normal to the naked eye.

The pia and arachnoid were œdematous, but no distinct exudate was found. The gyri were very little flattened. Both lateral ventricles were greatly dilated and separated from the surface by a thin layer of brain tissue only (about 3 cm. to 4 cm.). The cerebellum was small, and in consistence cartilaginous. The rest of the brain, was, if anything, soft.[1] On the cut surface the glia

[1] Regarding this point some divergence of opinion appears. The account of the autopsy was written to the dictation of the then (now deceased) chief physician, Dr. Wichmann,

tissue of the latent lobes seemed to be increased (the brain was sent to the Anatomical-Pathological Institute of the University of Copenhagen).

Case 4.—Gudrun Marie A. B., daughter of a bricklayer, born 1905, died February, 1907.

According to information from Dr. Kiær, in Hammel, the child, when visiting Hammel, was suffering from constipation. She is *the younger sister of the above patient*, was never admitted to the hospital, but treated at home by Dr. Bloch, who has given the following information :—

The disease was similar to that of her elder sister. The child was normal during the first months of her life, but then began to suffer from stiffness of the extremities and tonic cramps. Ophthalmoscopic examination was not undertaken. Frequent periods of elevated temperature occurred, during which the cramps grew stronger and the patient more debilitated. No stethoscopic changes nor intestinal symptoms were discovered during these periods of elevated temperature; on the other hand, vomitings were of frequent occurrence throughout the disease. She lived somewhat longer than the other patients and was $1\frac{1}{2}$ years old when she died.

The parents taking an interest in knowing whether or not the child had suffered from the same affection as her elder sister, Dr. Bloch was permitted to perform the autopsy at the home; the result was as follows :—

Brain (figs. 6 to 7) and spinal cord remarkably hard, almost cartilaginous, but did not present any abnormal configuration. The brain was placed in formaldehyde. When examined now (seven years later) the brain showed the following appearance to the naked eye : it was normal in shape and showed no macroscopic defects. It deserves to be mentioned that the shape had been so perfectly preserved that the organ had not flowed out by its own weight, as is usually the case with children's brains, but had remained remarkably hard, even before fixation. On the photograph (figs. 6 to 7) it is seen that the medulla oblongata straddles in the air, an unusual condition for a child's brain. On palpation the consistence of the cortex is found to be normal, whilst the white matter is extraordinarily hard—much harder than usual in a brain hardened in formaldehyde. This hardness is uniform throughout the organ. On the cut surface the cortex appears to be of normal colour and thickness, and is distinctly marked off towards the white matter, which is apparently somewhat diminished and of a reddish, somewhat marbled, grey colour. Immediately under the cortex lies a thin layer of substance which is still white.

whilst the then assistant physician, Dr. Bloch, also took part in the autopsy. He informs me that, according to his view, the rest of the brain was also extremely hard, though not quite as hard as the cerebellum. There is, on the whole, some reason to suppose that the process was not quite so far developed in this case as in the four other cases, as evidenced by the following circumstances : (1) the normal ophthalmoscopic appearances : (2) the severe gastro-enteritis, which in all likelihood caused the death at an earlier point of time than in the other cases.

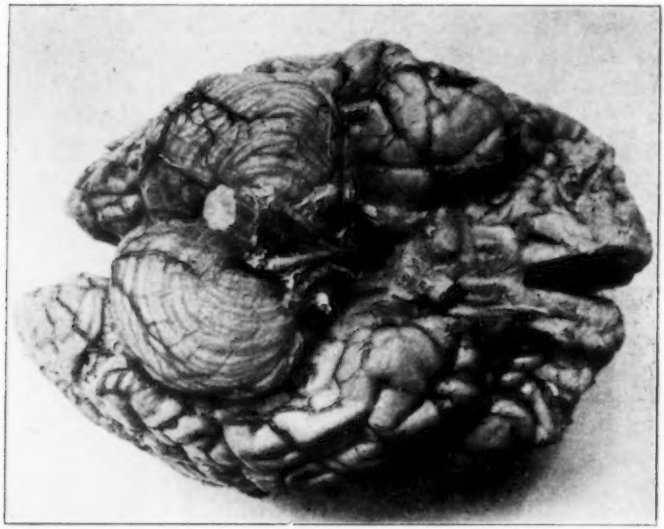

FIG. 6.—The brain of Case 4, Gudrun A. B.

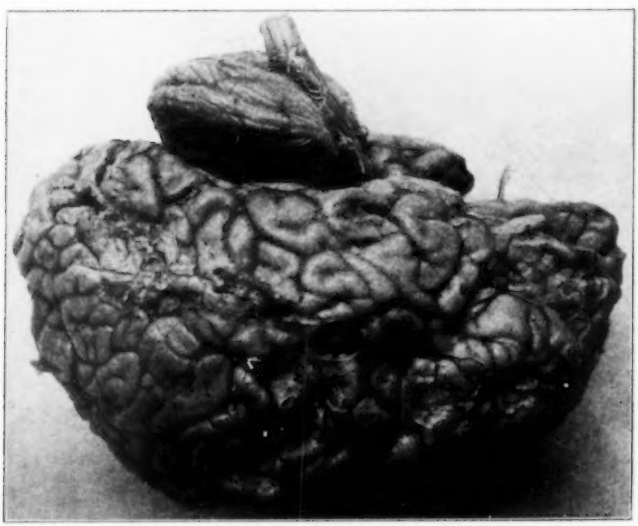

FIG. 7.—The brain of Case 4, Gudrun A. B.

Pieces of the brain were prepared: smaller sections for transference into chrom-acid acetic-acid mixture for the purpose of acid-fuchsin—vert-lumière staining, and larger slices, which were treated with Weigert's brown chrom-stain, and stained according to the methods of Kulschitzsky-Wolters and of Pal. When examined under the microscope these specimens, representing all regions of the brain, were found to contain changes (figs. 8 to 10). The white matter of the cerebrum, excepting a thin subcortical layer, was almost completely destroyed. The nerve-tracts in the pons were fairly preserved. Corresponding with the destruction of the medullary sheaths, an enormous increase of glia-tissue with large protoplasmic glia cells and infiltration of the vessel sheaths with scavenger cells was seen. As in Case 2, these cells for the most part were filled with fatty granules.

Case 5.—Frederik Ernst Ed., son of a baker, born October 12, 1905, died at the age of 11½ months.

Family history: Parents healthy, patient second of a family of two. The elder was healthy (according to later information subsequent children were also healthy). The patient was fed on nothing but the breast until admission to the hospital. During the first three to four months he was fairly well and thrived well. Then for some time he began to suffer from constipation; a fissure of the anus necessitated division of the sphincter. After this his condition improved and stools occurred spontaneously. Shortly afterwards, however, attacks of screaming and tetanic rigidity of the upper and lower extremities appeared. Now and then there was transitory elevation of temperature. Patient looked dull, and there was a peculiar smacking and masticating motion of the mouth, and moving of the tongue forwards and backwards. Examination of the chest and urine showed nothing abnormal. At the age of 6 months a kyphosis appeared in the dorsal region. The patient grew somewhat more quiet, but was admitted to Dronning Louise's Hospital (Queen Louise's Hospital for Sick Children) on May 23, 1906.

Physical examination then showed: Weight in full, 5,050 grm.; circumference of head, 43 cm.; circumference of chest, 38½ cm.; temperature, 37·5° C.; pulse 140. Urine contained much urates, but no albumen nor sugar. State of nutrition rather good; no signs of rickets. Skin greyish and cool; fontanelle normal; no gaping sutures. Ears and fauces normal; stethoscopic examination normal; glands in the neck only just of the size of a pea. Abdomen normal; liver and spleen not palpable. Pupils equal, active to light; no strabismus, sometimes pronounced nystagmus. No difficulty in swallowing. The nape of the neck was drawn backwards. Kyphosis of the spinal column in the dorsal region. Hands firmly clenched and only extended with difficulty. Arms reflexly bent at the elbow and resist extension. The legs are kept adducted at the hip-joint, stiffly extended at the knees, the right leg hyperextended at the knee and not flexible, whereas the left leg yields to flexion, though after great

Fig. 8.

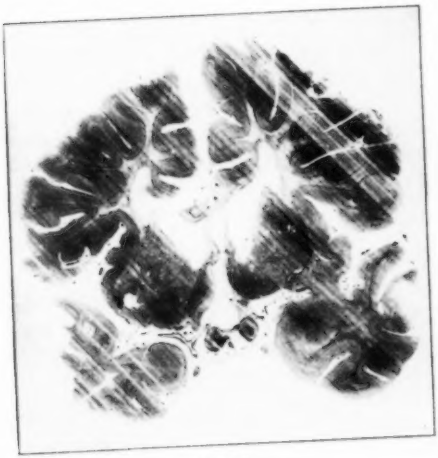

Fig. 9.

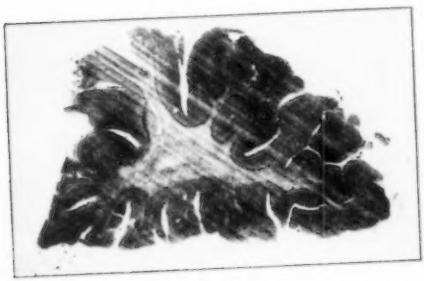

Fig. 10.

FIGS. 8 to 10.—Sections from the brain of Case 4, Gudrun A. B. Staining of Weigert-Kulschitzky-Wolters. For explanation of the figures see fig. 3, p. 79.

resistance. The feet are slightly in the equinus posture; they are not cold or œdematous. Patellar reflexes not obtained, no clonus of the foot. Periodic attacks of strong tonic rigidity, followed by screaming. Lumbar puncture on June 30: no fluid obtained.

The course of the illness during the six months' stay at the hospital was as follows:—

Temperature being at first normal, rose after a few days.

The stools at first were rather thin and gritty; later on they became normal, and remained so (July 3, 17 and 18 excepted). On September 17 the child began to get thinner. Vomiting occurred frequently once or twice daily; sometimes, however, the food was simply returned. The weight at first was increased from 5,050 grm. to 5,200 grm., then it fell rather evenly to 4,300 grm., and during the following months kept oscillating between 4,450 grm. and 4,300 grm. Finally it dropped to 4,000 grm. The urine was never found to contain albumen or sugar. In the beginning the patient was fed on milk and milk-pottage: later, on infants' food and barley water.

The following notes as to further course of the disease were taken from the ward journal:—

May 28: Condition not improved. Lies dozing most of the day; the spastic stiffness does not even cease during the sleep.

June 17: Ophthalmoscopic examination (Dr. V. Hertz) shows small equal pupils, active to light. As a rule, spasms of the downward movements. Under homatropine the discs were found to be bluish (probably physiological). The nasal edges were blurred, the veins strongly congested.

July 10: Mostly dozing, only cries when touched; no convulsions; nystagmus; no appetite; losing considerably in weight; no change of posture. Spastic hyperextended lower extremities, the head drawn backwards, and the back bent in the dorsal region; the hands clenched. Pupils equal; active to light.

July 25: Not able to swallow; nearly always dozing; purulent catarrh; lips dry.

August 31: Ophthalmoscopic examination: Pupils as before small, equal, active to light. Discs pale, especially in the left eye, veins prominent, nasal half more normal than before.

September 5: Nystagmus less pronounced than before. The spastic hyperextension of the lower extremities is unchanged. Upper limbs flexed at the elbows, hands clenched, stiffness of the neck, and curving of columna in the dorsal region. Fontanelle not distended, sutures firm. Circumference of the head, 43 cm.; circumference of chest, 37 cm.

September 28: Died at 11.30 p.m.

Autopsy fifteen hours after death showed abundance of serous fluid in the subdural cavity. Dura in some places adherent to pia; scattered smaller hæmorrhages. Pia not clear, somewhat œdematous. The lateral ventricles normal. The brain apparently rather diminished in size, but of normal shape. Consistence hard, almost cartilaginous. The cerebellum was in the same

condition. On the cut surface the glia tissue appeared to be increased. No further abnormality to naked-eye examination.

The posterior and basal portions of both lungs showed early infiltration. The mucous membrane of colon was swollen; the follicles stood out distinctly. Ductus Botalli closed.

Among the five cases described above, two (Cases 1 and 2) resembled one another so closely, both from the clinical and pathological aspect, that they obviously belonged to the same group. Case 4 must also be added to this group from the anatomo-pathological aspect, and, according to the rather imperfect description, from a clinical point of view as well. In Case 5, no microscopical examination was carried out, but the clinical picture, the naked-eye appearances and the consistence of the brain, entitle us to refer this case, too, to the same group.

With regard to Case 3 it may be maintained that—(1) the clinical picture bears a close resemblance to that found in the other cases (stiffness, spasms, &c.); and (2) it revealed the same macroscopical changes as those mentioned above, at any rate as far as the cerebellum was concerned. In considering the fact that in this case the rigidity remained unchanged till death, and that a severe dyspepsia was present, the most natural conclusion will be to rank this case along with the four others; this patient seems to have suffered from the same disease as the others, but owing to the gastro-intestinal complications died in an earlier stage, before the brain was fully sclerosed.

Summary of the Clinical Findings of the Cases.

The clinical picture of the above cases is very characteristic, but I should not dare to use it as the only point of support for diagnosis.

The first peculiarity about these cases—the family occurrence—will be discussed later on.

A characteristic feature of all the five cases is their acute onset at the age of 4 to 6 months in children who up to then had always been quite healthy. Only in one case (Case 2) was the child said to have been extraordinarily stiff all the time; it is, however, questionable how much stress may be laid upon this statement of the parents. As prodromal symptoms of the disease, causeless fits of crying and screaming were noted. Among the typical symptoms is the universal rigidity of the musculature of the body and the limbs, most pronounced in the lower extremities. A further stage of this rigidity is shown by the universal tonic spasms, which appear to be evoked by such stimuli as noise, light, or touching.

During the attacks the patients generally show the following posture: the head bent backwards, the back curved in opisthotonos; in Case 3, however, only the lumbar region was in lordosis, strong kyphosis being present in the dorsal region. The upper extremities are flexed at the elbow-joint, the hands in some cases clenched, in other cases placed in the obstetrical posture. The lower extremities are extended at the hip-, knee-, and ankle-joints, often adduced until they cross. As far as the cranial muscles are concerned, the spastic attacks were less pronounced. In two cases strabismus convergens was observed from birth and throughout the course of the illness; it did not, however, seem to increase during the attacks. In Case 5, on the other hand, no squinting was noted. In all cases nystagmus occurred, especially during the fits, and did not decrease till towards the end of the illness.

More difficult to settle is the question whether or not the muscles of the face were influenced by the spasms, as during the fits the patients cried and screamed violently. To the observer this conveyed the impression that the cries were a real reaction to the pain caused by the fits. The frequent occurrence of yawning in Case 3 may possibly be regarded as a spastic phenomenon of similar origin. The difficulty in swallowing occurring towards the end is rather a paralytic than a spastic phenomenon.

In addition to these attacks of tonic spasms, which seemed to be a higher stage of the permanent rigidity, regular eclamptic attacks, accompanied by strong clonic convulsions, were noted in several cases, although not very frequently. True paretic symptoms did not manifest themselves till towards the end of the disease, when the spastic condition gradually passed into a relaxed paralytic state. In Case 3, however, the rigidity remained till death.

It was impossible to make any observations on the sensory side. In Cases 2 and 3 there was at first reaction to pain, and in all cases reaction to all such pains as accompanied the convulsions. The presence of ataxia could not be determined, as the movements were at first so intensely spastic and then paretic that the patients were able to catch things (except in Case 1).

With regard to the sense organs, hearing seems to have been unaffected at first, as the patients were very sensitive to sound. In Case 2 this reaction was lost at the end. Sight, so far as Case 1 is concerned, was present for a few months, the patient being able to follow things with her eyes. The ophthalmoscopic results were, as a rule, characteristic; in three cases (1, 2, and 5) optic nerve atrophy

was observed, in Case 5 neuritis. In Case 4 no ophthalmoscopic examination was performed, and in Case 3 it gave a normal result. This, as already mentioned, may be due to the fact that the patient died before the affection had reached the same advanced stage as in the other four cases. The optic atrophy, therefore, seems to us to be a characteristic symptom, at any rate in the latest stages of the disease, and probably a sign of great diagnostic significance. The pupils in all cases were active to light, even in the latest stages (?). In Case 2 only was the reaction sluggish, and later on almost extinguished. The tendon reflexes of the upper extremities only are mentioned in Case 1 and described as brisk, whereas in none of the cases could the patellar reflexes be evoked, probably on account of the rigidity. As to the plantar reflexes, nothing can be judged from the notes at hand.

Restlessness and screaming were the chief symptoms in the beginning, succeeded by dulness. The mental faculties did not develop after the disease had begun. As a last sign pointing to the conditions of the central nervous system, the fontanelle presented a characteristic want of distension, and it was generally distinctly sunken.

In the periodic elevations of temperature (fig. 11) we find a symptom, the significance of which is not easy to interpret. In Case 3 the permanently elevated temperature probably must be ascribed to the dyspepsia, but in all the other cases no affection was found of the digestive tract, of the lungs, or of the urinary system, to which the short febrile periods might have been referred. In fact, they may be due to some occult infection or intoxication, and thus be regarded as a merely accidental complication. But, on the other hand, they may represent a characteristic feature of the disease, and thus be due either to an influence acting upon the temperature-regulating system or to the fact that the destruction of nervous substance, being the fundamental process of the disease, takes place at intervals, and causes elevation of temperature due to products of its destruction. It is, however, a matter of difficulty to judge from the ward journals as to the cerebral symptoms during febrile periods. According to the statement of Dr. Bloch, these periods were followed by aggravated cerebral symptoms; in Case 4 the convulsions and the screaming were far more pronounced during the duration of the elevated temperature, and in Cases 1, 2, and 3 this also seems to appear from the notes.

Great lowering of temperature was succeeded by coldness, debility, even by collapse and sometimes by eclamptic fits (Case 1). In Case 3, however, eclampsia also occurred outside the periods of subnormal

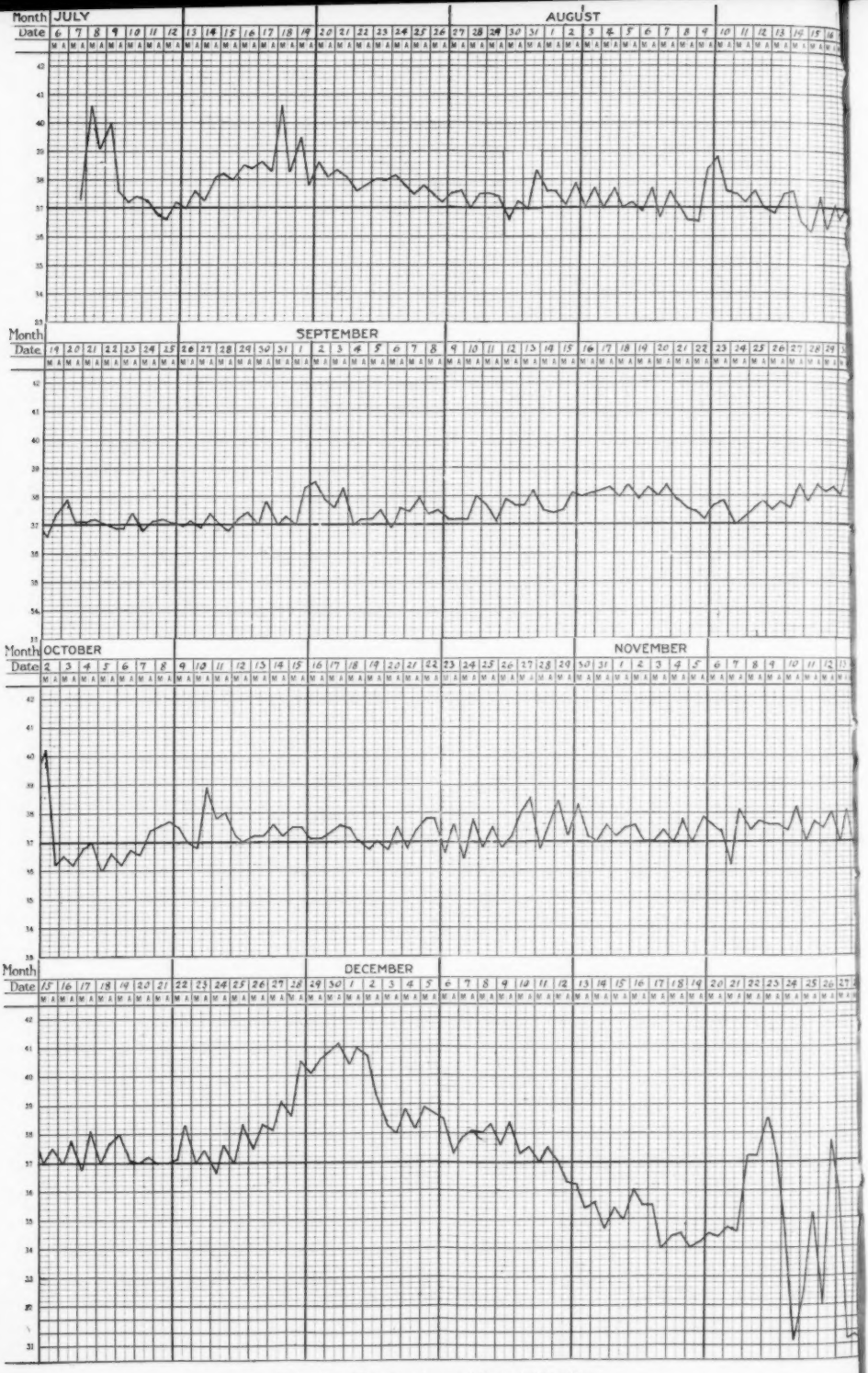

FIG. 11.--Temperature of Case 1 (Kai Bu.).

temperature. All the cerebral symptoms, the vomiting excepted, can be regarded as more or less casual complications. The vomiting was of rather frequent occurrence in the four last patients, but did not appear in Case 1, in which only slight regurgitation was noted. Diarrhœa occurred in Cases 1 and 5 a few times, in Case 2 not at all, but in Case 3 was almost permanently present, the stools being of a thin and mucous consistence. Here the dyspepsia probably had given rise to the albuminuria (the œdema), the stomatitis, the pharyngitis, the catarrh, the eczema and the conjunctivitis; some transitory catarrh and conjunctivitis in Case 5 and some pyuria in Case 1 excepted, no such severe complications were found in the other cases.

No affection of the heart nor the lungs occurred except the terminal pneumonia. The weight as a rule oscillated, decreasing during the latter period. The terminal increase of weight in Case 3 was due most probably to retention of urine.

It may be added that lumbar puncture and Wassermann's reaction, performed in two cases, gave negative results.

Anatomo-pathological Considerations of the Cases.

The most characteristic feature of the above cases, as far as their pathological anatomy is concerned, is the complete destruction of the axis-cylinders and medullary sheaths, the replacement of the destroyed tissue by neuroglia and the relative intactness of the nerve-cells. The destruction shows a peculiar distribution, as may be seen from the description of Cases 1, 2 and 4; the processes of all the nerve-cells of cortex cerebri and cerebelli are most affected; destruction of the processes from the basal ganglia represents the next stage and of those from the spinal centres the last stage of the disease.

This affection probably proceeds evenly, as, had it been of sudden occurrence, cysts and irregularity of the glia proliferation would have been present. The regular distribution of glia tissue without any deformation of the brain is most naturally explained by the steady substitution of glia in places where the nervous tissue was destroyed.

Furthermore the process must be looked upon as being no longer progressive in Case 1, and as nearly ended in Cases 2 and 4, on account of the extraordinarily scanty Marchi degeneration in the first case, and from the small number of fatty and of albuminous granules in the scavenger cells. To reconstruct the onset of the process from the existing pathological changes is, however, rather difficult, although it may be possible to draw some conclusions as to certain facts. The question is,

whether the affection is to be regarded as—(1) a variety of tumour-growth, (2) a repaired inflammatory process, or as (3) a simple degeneration of the nerve-cell processes.

The first explanation, that it is a kind of gliomatous formation, is entirely untenable. It is quite impossible that a tumour could occupy nearly all the white matter of the central nervous system, and abruptly terminate where it approached the grey matter, causing no deformation of the brain.

The explanation that it is due to an inflammatory process appears to be more probable, provided that we allow that when the presumed inflammation has passed away no infiltration with plasma cells, lymphocytes, or polynuclear leucocytes is traceable anywhere. In my opinion, the strict limitation of the lesions to the white matter seems to speak against an inflammation. Another objection to the theory of an inflammation in these cases is the peculiar distribution of the changes within the white matter. There is no distinctly marked focus, but a selective destruction which predominantly affects the processes of the cortical pyramidal cells, leaving the adjacent regions of the white matter, as, for instance, the tracts of pons, undamaged.

A third point of significance seems to me to be a comparison of the above cases with the one previously described by me under the name of "perivascular necrosis of the medullary substance." As was already emphasized in the previous paper, the changes—(1) were only found in the medullary substance, and not in the grey matter; and (2) consisted of a slight diffuse destruction of the medullary sheaths throughout the white matter and of a complete disintegration of the vessel sheaths. Corresponding with this was found—(3) a protoplasmic and partly fibrillary glia and great quantities of fatty granule-cells round the vessels, carrying away the decayed myelin sheaths.

This picture, in fact, corresponds exactly with the initial stage of the above cases of diffuse sclerosis. The age of the child being nearly the same, and other points of resemblance being present in the clinical history, I feel myself entitled to consider this case as an initial stage of those described in this paper, but a stage which was interrupted by death owing to gastro-enteritis.

If I am right in maintaining this assertion, it must also be supposed that the disease is not of inflammatory origin, as in the said case neither leucocytes nor lymphocytes nor plasma cells were found anywhere.

I am compelled, therefore, to refer the disease to a mere degenera-

tive process. I feel, however, inclined to alter my conception regarding the case previously reported. The fact that the destruction of the medullary sheaths was predominantly round the blood-vessels, and of a more scanty occurrence towards the periphery, was indicative of a perivascular origin of the process, and the slighter disintegration in the outer regions I referred to a secondary degeneration of such medullary sheaths as pass near the vessels.

This, however, might also be explained in the following way: the degeneration of the medullary sheaths sets in diffusely, and the more intense destruction round the vessels is due to the fact that the glia-cells, receptors of the products of destruction from the degenerated sheaths throughout the white matter, wander into the vessels and push aside the surrounding sheaths.

Which of these explanations may be acknowledged as the right one is difficult to decide. In the case here described the density of the fibrillar glia was more pronounced round the vessels than at some distance from them. But this dense glia only appears as a comparatively thin and sharply limited tube round some of the blood-vessels. The explanation might therefore just as well be based upon the supposition that the glia becomes particularly dense in places where the protoplasmic glia-cell wanders, carrying with it the products of destruction.

We are thus, on the whole, more inclined to believe that the perivascular destruction of the medullary sheaths and heaping up of glia-cells is not the primary but the secondary factor and the natural consequence of the diffuse destruction of the medullary sheaths and axis-cylinders. No final decision can be reached until a case has been examined which is more advanced than my first case.

In this place I might mention a case to which my attention was not drawn till after the completion of my first paper; this case was reported by Lewandowsky and Stadelmann, and a *post-mortem* examination showed a recent affection of the brain. The most characteristic feature was a heaping-up of glia-cells distributed in spots, but with no inflammatory symptoms, and the axis-cylinder processes were not preserved in places where the medullary sheaths were destroyed, as is the case in disseminated sclerosis. The patient in this case being an adult, I must, however, in spite of the parallel, look upon it as different from my own.

I have now come to the third possibility, which to my view is the most probable, namely, that the affection is a merely degenerative process, analogous to such degenerations as are frequently found in certain hereditary or familial nervous affections, as, for instance,

Friedreich's disease. This interpretation is not only based upon the advanced destruction of the medullary sheaths and of the axis-cylinders traceable without any signs of inflammation, but it chiefly rests upon the characteristic distribution of the degenerative processes. These, to a certain extent, are just as selective as the degenerations in the hereditary nervous diseases; the tracts destroyed consist of all the axis-cylinders of the pyramidal cells of the cortex cerebri and the cells of the cortex cerebelli, together with their medullary sheaths. Corresponding with this, the degenerations met with in the central part of the brain and in the spinal cord mostly affect the pyramidal and cerebellar tracts, whereas the spinal nerve tracts are relatively intact, and the nerve processes from the centres of the spinal cord are all but undamaged.

I therefore believe that the degeneration of this enormous amount of nerve tissue is the primary factor of the disease, whereas the glia proliferation and the infiltration of the medullary sheaths with the gliogenous fatty granule-cells and other scavenger cells represents a secondary process.

EXPLANATION OF FIGURES.

Figs. 12 to 16 are stained with Alzheimer's acid-fuchsin.

Fig. 16 with Alzheimer's staining with Mallory's hæmatoxylin. The background fibres are neuroglial fibres. All the sections are from Case 1, Kai Bn. The figures are drawn by the author with a Zeiss's microscope, ocular ii, objective immersion $\frac{1}{12}$.

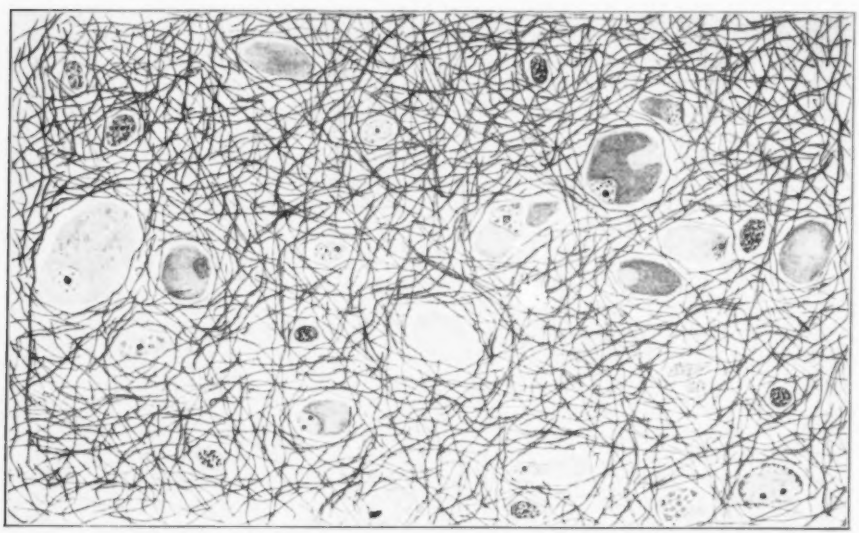

FIG. 12.—White substance of the hemispheres. The whole white substance is replaced by neuroglia in which may be seen many different types of neuroglial cells, small and large.

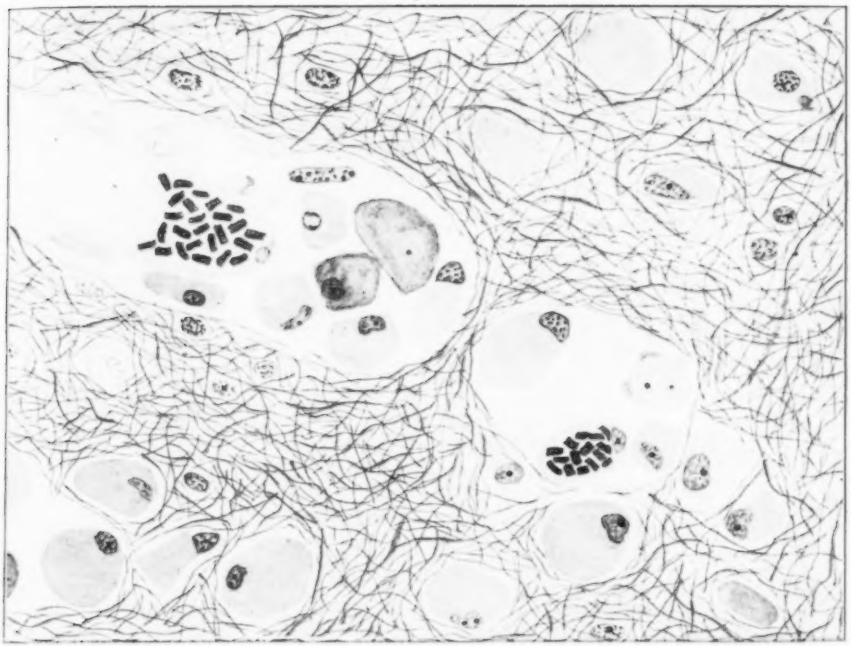

FIG. 13.—White substance of the hemispheres replaced with neuroglia. Two vessels can be seen (the erythrocytes are stained red) surrounded with gliogenous "scavenger" cells.

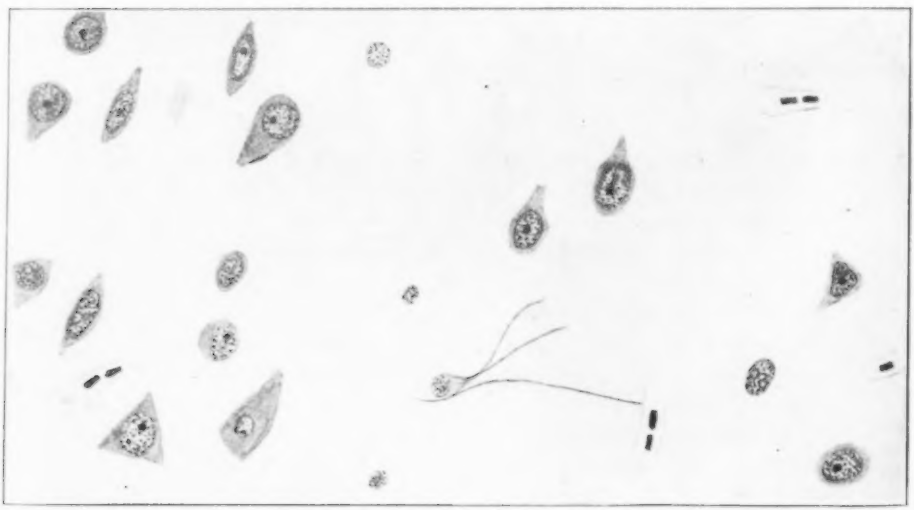

FIG. 14.—Grey substance of the hemispheres. The nerve-cells seem normal, and there is no augmentation of the neuroglia; only one neuroglia cell with fibres is seen.

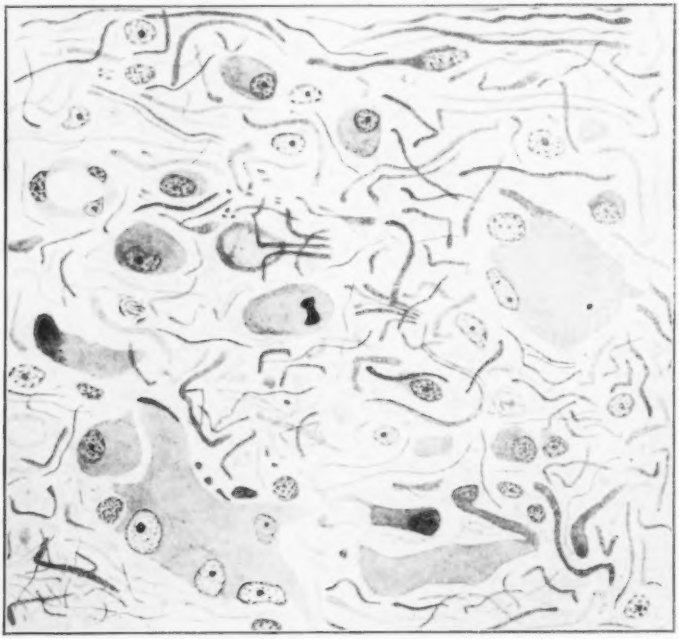

FIG. 15.—Partly from the internal capsule; the white substance is replaced by abnormal neuroglia, gigantic polynuclear glia-cells with big fibres and degenerated nuclei.

THE NOSOLOGICAL PLACE OF THE DISEASE.

The above five patients, and probably the one previously described by me, present so many points of resemblance from a clinical and especially from an anatomo-pathological point of view, that it can scarcely be doubted they belong together. The most conspicuous feature, as far as their pathological anatomy is concerned, is the extraordinary hardness of the white matter of the brain and the spinal cord.

Several cases have been reported in the literature under the name of diffuse sclerosis of the brain, in which the main characteristic has been just such hardness of the brain. In fact, no other cerebral affection presents a similar hardness, and I thus feel entitled to classify my cases temporarily in one disease-group.

On the other hand, it may be considered beyond doubt that such sclerosis of the brain in most cases represents the final stage of various processes which are pathogenetically different, and previous authors

have tried to discriminate special forms within the category of diffuse sclerosis of the brain. One of the most prominent papers on this subject is written by Schilder. He not only gave a detailed report of the clinical and pathological findings of his own case, but also instituted a re-examination of the literature, and called attention to the cases

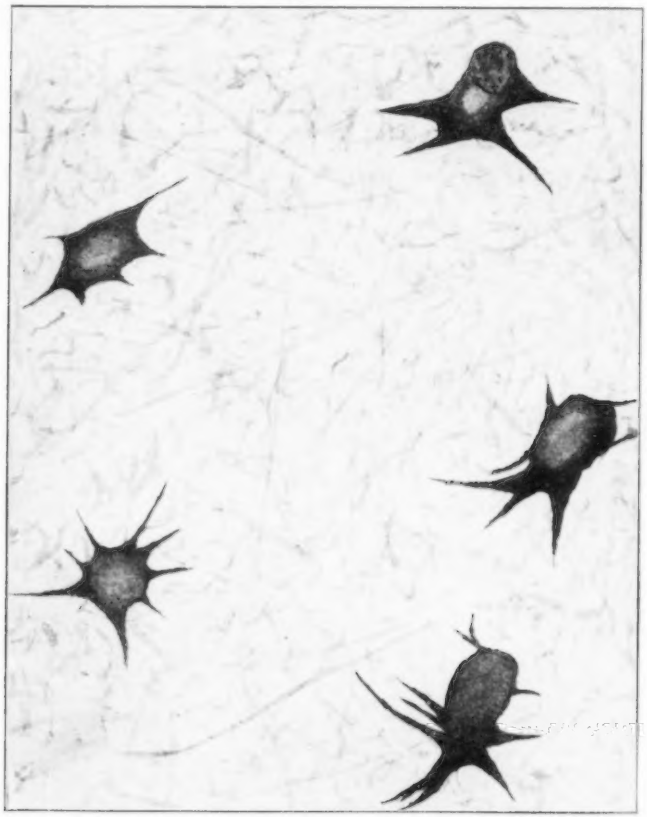

FIG. 16.—White substance of the hemispheres replaced with neuroglia. Shows the spider-cell forms.

already described as diffuse sclerosis of the brain; he gathered together such cases as have been published under other names, but which should be referred to this group. He thus separates four cases as a special group under the name of encephalitis periaxialis diffusa, considering them to be related to the disseminated sclerosis.

My cases, however, present certain peculiarities in which they differ considerably from the cases described by Schilder; thus they began in babyhood, they tended to occur in families, and they showed a complete absence of any signs of primary or secondary inflammatory processes. In the literature I have found one case—viz., Beneke's—which may be classified with the cases reported in the present paper.

Finally, there are certain cases reported in literature of syphilitic origin; but no syphilitic origin existed in Schilder's case or in my cases, and these syphilitic cases fall into a group by themselves.

In the following pages I shall discuss these three groups, giving, however, but a brief summary of the first and second group, whereas of the third a more detailed report will be given. I only refer to the disease in children.

Group I: the syphilitic.—It is no easy task to draw the line between syphilitic and the non-syphilitic cases. Some of the cases of the next group are probably syphilitic in origin, such cases, for instance, as are antecedent to the Wassermann reaction and where syphilis was present without being noted in the history. On the other hand, cases in which Wassermann's test proved positive, or cases in which syphilis was discovered in the history, might be ascribed to casual complications. Considering the varying forms under which syphilis generally appears in the central nervous system, I should, however, think it the most natural solution to explain these cases as syphilitic.

The first group, then, comprises the following cases:—

Buss: Hereditary syphilis in a child aged 2 years 6 months. Strümpell's case, in which the father suffered from typical tabes dorsalis. Haberfeld and Spieler's second case, in which the mother was syphilitic; and finally the case, reported and illustrated by Zappert, in the chapter on the central nervous system in the "Text-book of Pfaundler and Schlossmann," and a case observed by Pfaundler, in which syphilis was present, consanguinity of the parents, and paralysis of the father. Although the evidence of syphilis in these cases is not always to be relied upon, the disease must still be referred to a syphilitic affection, and the more so as *post-mortem* examination in several cases showed no particular limitation to the white matter, but an extension to the grey matter, combined with grave changes in the ganglion system, or with chronic meningitis. The case described by Bullard may also be placed among the syphilitic affections, which, although no history of syphilis was present, microscopically resembled general paralysis.

Group II: encephalitis periaxialis diffusa.—The second group comprises cases for which Schilder has proposed the name of encephalitis periaxialis diffusa, and which are in his opinion related to disseminated sclerosis. As to the relationship I shall not express myself any further, Schilder having thoroughly discussed the reasons for and against. On the whole, we may agree with the conception that some cases of diffuse sclerosis of the brain are especially extensive disseminated sclerosis. Schilder himself places in this group, in addition to his own case, the cases reported by Rossolimo, Ceri, Haberfeld-Spieler and Beneke. For reasons which will be discussed later on, I should, however, feel inclined to refer the last case to the next group. There are, moreover, a number of cases which may well belong to this group, in spite of the pathological-anatomical description not being always detailed enough to permit any sure definition of the disease. This, for instance, applies to the cases reported by Schüle, Longkamp (first case) and Meine. A copious description of the chief characteristics of these cases having been already given by Schilder, I shall only here refer to his paper.

Group III: the familial early infantile form of diffuse brain sclerosis.—Regarding the pathogenesis of our cases and their place within the nosology, it may at first be noticed that they are absolutely different from the syphilitic group; there was no clinical evidence of congenital syphilis, and the pathological-anatomical findings differed from those found in syphilitic lesions. My cases differed, moreover, fundamentally from Schilder's encephalitis periaxialis diffusa. This affection, as a rule, seems to be indicative of a reparative inflammation, and the process does not affect the whole central nervous system; but as far as the cerebrum is concerned it appears to be confined to certain regions. The disease sets in during later infancy, and is of no familial occurrence. Against the latter assertion, however, Halberfeld and Spieler's case may be quoted, in which a relative of the patient was said to have been subject to the same disease. Let it be remembered, though, that this statement was due to the parents and not to the physician, for which reason the family occurrence may be regarded as somewhat doubtful. The process in my cases has been degenerative and not inflammatory, and affected the whole cerebrum and cerebellum; it always began during the first six months of life, and in four out of five cases presented a familial occurrence.

All these conditions point away from encephalitis periaxialis diffusa, and are totally unlike any form of disseminated sclerosis. Furthermore,

disseminated sclerosis is very rarely of familial occurrence; in fact, authors such as Müller will not acknowledge cases of familial appearance as disseminated sclerosis. Finally this disease is very seldom found in children; among fourteen cases reported by F. Wolf (1912), only one (the author's own case) could be traced back to the first year of life, and this, too, must be considered very doubtful. At any rate, the diagnosis was not verified by autopsy.

The pathological-anatomical findings, however, and the familial occurrence point to another group of diseases—namely, the hereditary familial nervous affections. The isolated occurrence in Case 5 is of but small importance, firstly because all familial diseases may appear sporadically, and secondly because the case, on the whole, is in perfect keeping with the other cases as far as the clinical and pathological findings are concerned.

It is equally evident that there is just as deep a separation between my cases and Schilder's encephalitis periaxialis diffusa as between Friedreich's disease and disseminated sclerosis.

In attempting to place my cases of hereditary familial nervous affection, the point is, to which of these groups are they most intimately related? The two groups of disease to which my cases may belong are, on the one hand, Pelizaeus-Merzbacher's disease, aplasia axialis extracorticalis congenita, and on the other, Tay-Sachs' type of familial amaurotic idiocy.

My cases resemble aplasia axialis extracorticalis congenita in that they set in during the first years of life, and show pronounced destruction of the white matter of the brain. But there is a considerable difference in the clinical picture and in the course of disease. Aplasia develops to a certain point and then remains stationary. In my cases the pathological process, on the contrary, advances inflexibly and relatively quickly until a fairly complete destruction of the white matter of the cerebrum is produced. In this respect my case presents a kind of the relationship to familial amaurotic idiocy. This, on the other hand, forms a supplemental contrast to my cases, the most characteristic feature being the degeneration of nerve-cells, whereas it is the destruction of the axis-cylinders and myelin gains which characterize my cases.

It is universally recognized that there has been a somewhat exaggerated tendency to divide the familial nervous and muscle diseases into a countless number of types representing only transitional forms. It seems to me, however, that my cases show pictures so typical and distinct from all other cases, even from Pelizaeus-Merzbacher's disease,

that I am entitled to regard them as a special group within the familial nervous diseases, and, in fact, a group to which the name of *familial early infantile brain sclerosis* may rightly be given.

The next question of interest is, which of the cases previously described in the literature ought to be referred to this group? The most minutely reported case is that of Beneke, but unfortunately it contains no clinical history, only a pathological-anatomical description.

Beneke's case was a boy aged 1 year 9 months, 51 cm. in length. *Post-mortem* examination showed a double-sided pneumonia, ecchymoses on the abdomen, and contraction of the elbow-joints, but otherwise no abnormality, except in the central nervous system. The pia was hyperæmic and œdematous. The shape of the brain did not show much change other than a great increase of consistence. This increase was also found in the basal ganglia, in the bulbus olfactorii and in the optic nerves. In the cerebrum itself there was no sclerosis of the cortex, but only of the white matter and, to a certain extent, of the basal ganglia and the central nuclei, such as the nucleus caudatus, claustrum, &c. In the cerebellum an extensive sclerosis was noted coincident with a soft focus in the cortex. There was no encephalomalacia. The spinal cord was also intensely sclerosed. The sclerosis did not seem to be total as in my cases—it consisted of large confluent foci intermingled with traces of white matter. As in my cases, a narrow streak of white substance, fairly undamaged, was found immediately under the cortex. The occipital lobes and the frontal lobes presented the softest consistence. When examined under the microscope the tissue was found to show a copious increase of glia corresponding to the grey foci. The cell types showed all transitional stages from glia cells without a protoplasm to large polymorphonuclear homogeneous cells with a peripheral arrangement of the nuclei. The latter forms were generally found in dense layers round the larger or smaller blood-vessels, or formed isolated punctiform groups in the middle of the glia tissue. The substance between the cells was hard, fine and densely fibrillated. Within the dense sclerotic regions, medullated nerve-fibres were found which had escaped destruction, mostly arranged peripherally. Everywhere fatty granule-cells were noted, but not in very great quantities. In contradistinction to this, the sclerosis of the spinal cord chiefly consisted of dense masses of glia-fibres without any special increase of the glia-cells. The fatty granule-cells were quite wanting here and some of the ganglion-cells were degenerated. The process seemed to be progressive in the brain, and finished in the spinal cord.

The author calls attention to the difficulty of proving whether the process might be an inflammation, a congenital anomaly of growth, or a kind of tumour formation; the analogous large cells can be found in many gliomata, and also in regenerative processes.

Beneke's report seems to correspond with my cases in all essentials, the only difference being that the process was not so advanced here as in my cases. The child is presumed to have died during the development of the affection.

Among other reported cases from early infancy two only can be referred to this group—namely, the cases reported by Schmaus and by Heubner. In both cases, however, the patients were somewhat older children (Heubner's, aged 5; Schmaus's, aged 3). The pathological-anatomical findings do not permit me to classify them with certainty. It may be added that in none of these three cases were other members of the family affected.

As will be evident from this review of the literature, not many cases are recorded in early infancy, and it therefore appears remarkable that Zappert, in "Pfaundler Schlossmann's Text-book," states that the disease is of frequent occurrence in small children. ("Vorwiegend werden von der diffusen Sklerose Kinder in den ersten Lebensjahren selten grössers Kinder, oder Erwachsene betroffen.")

Nearly all his references to literature apply to adults or to older children.

Summary and Conclusions.

(1) The so-called diffuse sclerosis of the brain in children may be divided into at least three quite distinct types: (i) A syphilitic form; (ii) Schilder's encephalitis periaxialis diffusa; (iii) a familial infantile form, of which five cases are discussed in the present paper; the literature probably contains one other case.

(2) This form shows the following characteristics: it is usually a familial disease; it sets in somewhat acutely in about the fifth month in a child who up to then has been quite healthy; it progresses on a chronic course, ending with death, five to six months after the onset; universal rigidity of the musculature, violent tonic spasms, probably causing pain, and brought on by touching or noise form characteristic symptoms. As a rule, nystagmus is present, and in the latter stages atrophy of the optic nerve. Periodic elevations of temperature occur without perceptible cause, outside the central nervous system. Finally, extensive paresis and pronounced debility close the scene.

(3) The pathological-anatomical findings are: a marked hardness of the white substance of the brain without alteration of its shape. Microscopical examination of three cases showed relative intactness of cortex and the basal ganglia, the nervous centres of the brain and of the spinal cord; destruction of the medullary sheaths and axis cylinders throughout the white substance of the cerebrum (a 2-mm. layer, however, is preserved immediately under the cortex). Complete destruction of the white matter of the cerebellum and degeneration of the spinal nerve tracts are present. The destroyed tissue is replaced by dense fibrillar glia, in which are seen a considerable number of variously shaped glia-cells, mostly protoplasmic; the vessel sheaths are infiltrated with fatty granule-cells and other apparently gliogenous scavenger cells. There is a total want of new formation of vessels or infiltration of the vessel sheaths with plasma-cells, lymphocytes, or leucocytes.

(4) The affection must be regarded as a purely degenerative and not as an inflammatory process. The disease presents a certain relationship to Pelizaeus-Merzbacher's disease, aplasia axialis extracorticalis congenita, on one side, and to Tay-Sachs' form of familial amaurotic idiocy on the other side. In other respects, however, it differs conspicuously from both these groups.

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ACUTE POLIOMYELITIS.[1]

By F. E. BATTEN, M.D.Cantab., F.R.C.P.Lond.

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[1] The Lumleian Lectures, for 1916, delivered before the Royal College of Physicians of London.

Chapter I.—Introduction.

Mr. President and Fellows,—I would in the first place wish to thank the College for the honour they have conferred on me by their invitation to deliver the Lumleian Lectures for 1916.

The subject, acute poliomyelitis, is one which has not previously been dealt with by a Lumleian Lecturer, although a consideration of some points formed part of Farquhar Buzzard's Goulstonian Lectures, delivered in 1907 [33].

Since that date not only has poliomyelitis spread in epidemic form over the face of the globe, but considerable advances have been made in our knowledge of the disease. It is true that previous to 1905 small epidemics had occurred, but it is only since that date that it has had its present wide prevalence.

During the last six years the experimental investigation of Flexner and his co-workers at the Rockefeller Institute, of Levaditi at the Pasteur Institute, and Leiner and von Wiesner in Austria, and Römer in Marburg, have thrown much light on the nature of the disease.

A wider knowledge of the clinical manifestations has been gained, and the investigation of acute cases has rendered the pathological process more clear.

It is my purpose to put before you in these Lumleian Lectures the epidemiological, experimental, and clinical observations, and some points with regard to treatment of the acute stage of the disease.

It is during the last five years that poliomyelitis has been recognized by the Public Health authorities in England as a definite specific fever, and notification has been adopted. The British Islands have suffered comparatively little during the epidemic period.

Although much has been discovered with regard to its nature, it has not yet been possible to apply that knowledge to its prevention, and much investigation still remains to be done, not only in the experimental, but also in the clinical and epidemiological fields.

The likeness which the disease bears to rabies has raised the hope that precautions, which have been so successful in dealing with that infection, might be able to control poliomyelitis, but in its spread it bears such a likeness to that of meningococcal meningitis that this can hardly be expected. It seems unlikely, however, that any effectual remedy, other than prevention, will be found for a disease which is so fulminating in attack and so destructive in its effects on the central nervous system.

The first lecture will be devoted to the epidemiology and pathology; the second to the experimental side, and the third to the clinical consideration of the subject.

The names which have been used and suggested for the disease are numerous: spinal infantile paralysis, epidemic infantile paralysis, epidemic poliomyelitis, meningo-myelo-encephalitis disseminata, polio-encephalo-myelitis, Heine-Medinische Krankheit, acute anterior poliomyelitis, and acute poliomyelitis.

There is no doubt that the terms meningo-myelo-encephalitis disseminata and polio-encephalo-myelitis most accurately describe the anatomical and pathological changes; but the name "acute poliomyelitis" has now come into such general clinical use, and is used to describe the nature of the virus, that it is inadvisable to attempt to replace it. All that is required is that poliomyelitis shall be recognized as one of the acute specific fevers, having a tendency to affect any part of the central nervous system, and giving rise to a variety of symptoms dependent on the portion affected.

Epidemiology of Poliomyelitis.

(1) *Historical.*

The history of the earlier epidemics of poliomyelitis has been written by Allen Starr [26], Holt and Bartlett [12], who collected the records of thirty-five epidemics of poliomyelitis up till 1907, and further details were reported in the papers of Wickman [27], Job and Froment [14], and Sever [25].

In 1911 I collected additional records of some twenty-six epidemics in all parts of the world, and these, together with those previous to 1907, are recorded in a paper on the subject published in Brain of that year [1].

(2) *World-spread.*

The leading features of the past epidemics may, however, be shortly stated. The first record of the disease in an epidemic form came from Sweden in 1881. In 1883 some groups of cases were recorded in Italy, and in 1886 in Norway, Germany, and France. All these epidemics were small in numbers. In 1887, Medin described an epidemic in Stockholm of forty-four cases, and this is the first important work on the subject. In 1894 an epidemic of 132 cases occurred in Rutland, Massachusetts, which was recorded by Caverly and McPhail. Small epidemics were recorded in the "nineties" in Italy, France, Australia,

England and America, and a larger one occurred in Vienna (forty-two cases) in 1898, and in Norway and Sweden in 1899. This last was described by Wickman, to whom so much is due in regard to the investigation of the pathology and the spread of the disease. In the middle of the next decade—viz., 1900 to 1910—the record of cases, which before had been limited to two figures, now reached to four figures, and during the years 1903-07 it may be said that the disease was pandemic in Norway and Sweden. During the years 1907-10 large epidemics occurred in the States of New York and of Massachusetts. At the same time epidemics of the disease were recorded in Australia (Stephens), in Vienna (Zappert), Westphalia (Krause and Reckzek), in Paris (Netter), in Austria (Furnratt, Potpeschnigg, Lindner and Mally), Switzerland (Hagenback), and in Russia (Jogichess).

During the year 1910 the total number of cases and deaths from poliomyelitis in the United States was 5,093 and 825 respectively, a mortality of about 13·75 per cent. The epidemics in Massachusetts in 1909 and 1910 were most carefully investigated by Lovett [17] and his co-workers, and in Cincinnati and Batavia in 1911 and 1912 by Wade Frost [9], in regard to all the following factors: rainfall, temperature, surroundings, nearness to railroad, nearness to water, age of house, sanitary conditions, location of house, character of house, floor of house inhabited by a family, sewage disposal, character of water supply, relation to dust, prevalence of vermin, insects and rodents, data as to domestic animals kept, occurrence of paralysis in animals, swimming and wading, exposure to heat, cold or damp, diet, and attendance at school. No common factor could be found. No relation to dust, prevalence of vermin, or the keeping of domestic animals could be ascertained, and the same is true of the numerous other points investigated.

(3) *Factors common to all Epidemics of Poliomyelitis.*

There are, however, certain factors common to all epidemics, and these may be shortly stated.

Seasonal relationship.—In the Northern Hemisphere the disease always has the greatest prevalence during the months of July, August, September and October, the months of August and September being nearly always those in which the greatest number of cases occurs. In the Southern Hemisphere the disease has occurred during the months of March and April—i.e., months which, I believe, in atmospheric conditions correspond fairly well to September and October

in the Northern Hemisphere. The disease was supposed not to occur in the Tropics, but an epidemic was reported in Cuba in 1909 by Lebredo and Recio [16], the maximum number of cases occurring in July and August, and in the island of Nauru, in the Southern Pacific, in January, 1909, by Müller [20]. It is interesting in the latter epidemic to note that it affected the natives of the island very severely. In this island, which has a population of 1,250 natives and 1,000 imported labourers (partly Chinese and partly Caroline Islanders) and about 80 whites, there were 700 cases of the disease: of these 38 died; 470 of the 700 cases occurred in natives of the island, and of these 37 died. The Chinese were unaffected, and only three Europeans were attacked. So the disease fell with peculiar severity on the native population and the imported Caroline Islanders.

Age-incidence.—The incidence of the disease on young children is a constant feature, and it commonly attacks these during the second and third years of life. Babies in arms are rarely affected, and as the age advances the incidence rapidly declines.

Mortality.—The mortality in the various epidemics varies considerably; over the total number of cases it amounts to from 11 to 12 per cent. Of the notified cases in England during the years 1912-13-14, the mortality was 13 per cent., 14 per cent. and 16·6 per cent. respectively; but this hardly represents the true mortality, which is probably considerably lower, for it is certain that many of the milder and abortive cases are not notified.

Incubation.—In the Swedish epidemic of 1905 (Wickman) the incubation period was shown to lie between one and four days, seventy-four of the 127 cases coming within this period. Currie and Bramwell [8] brought forward some very good evidence from a small localized epidemic in Tillicoultry that it was four days or less. There are some striking individual cases of isolated contact which show that the incubation may be as short as twelve hours.

Spread of infection.—Wickman showed that the disease spread by means of carriers along the lines of communication—road, railways, &c. He brought forward evidence of the spread of infection from school. The school epidemic reported by Wickman occurred in Trästena, a little village of 102 houses, of which nineteen were affected. The school was infected by a child attending on June 28, and a series of cases which could directly or indirectly be traced to the school occurred on July 3, July 4, July 8, July 10, and July 12. The school was shut on July 15. Other cases occurred during the month, and the last on August 4.

In this little parish of Trästena, with 500 inhabitants, forty-nine persons were affected, twenty-three with the abortive form of the disease, twenty-six with the paralytic form. Of the cases with paralysis, eleven died—i.e., 42·3 per cent. Three other instances of a school being a source of infection are given by Wickman. The disease appears always to be carried by contact, but the "carrier" may be a perfectly sound and healthy individual. Further evidence on school infection was collected by myself in 1911, but although isolated cases of poliomyelitis occasionally occurred in schools in England, yet no evidence of spread from this source was forthcoming [2].

The disease rarely occurs or spreads in institutions. An investigation in America of forty-five institutions in which 3,600 children resided, showed that only one child contracted the disease during an epidemic period.

(4) *Poliomyelitis as an Epidemic Disease in Great Britain.*

So far as I know, there is no record of any epidemic of poliomyelitis in England before 1897, when W. Pasteur [21] described the affection in seven members of one family. That record has become historic, as it is the highest number of members affected in the same family.

Thomas Buzzard [6], in 1898, published a lecture "On Cases illustrating the Infective Origin of Infantile Paralysis." He gives an instance of two sisters residing in the same house who were attacked with paralysis within six days of each other. Four other children of the same family escaped. Two other children living in a neighbouring street were taken ill in a similar way in the same week. He also mentions a case, seen in 1895, of a brother and sister who were taken ill within two days of one another; the sister was feverish and recovered without paralytic symptoms, the brother was paralysed in the left arm. These two cases are alluded to in Buzzard's Presidential Address before the Clinical Society in 1895.

It has, of course, long been recognized that poliomyelitis is prevalent during the summer months in London, and especially during August and September. I recorded an undue prevalence in 1904.

In 1908 Treves reported an epidemic of eight cases at Upminster, a small village in Essex.

In 1909 an epidemic of thirty-seven cases was reported by George Parker in Bristol.

In 1910 Garrow reported cases of poliomyelitis in Cumberland, notably in Carlisle and Barrow-in-Furness.

Dr. Beard, the Medical Officer of Health in Carlisle, recognizing that the disease was occurring in an epidemic form, obtained the sanction of the Health Committee to make the disease notifiable.

NUMBER OF CASES OF POLIOMYELITIS IN ENGLAND AND WALES FOR THE YEAR 1912.

FIG. 1.—The figures indicate the number of cases of poliomyelitis notified in each county during the year 1912.

This, I believe, was the first place in which notification was instituted in this country. In this year epidemics also occurred at Melton Mowbray, Cerne Abbas [1] and around Edinburgh [18].

In 1911 numerous epidemics were recorded throughout England: notably in Devon and Cornwall and in the Eastern Counties [4]. That in Devon and Cornwall was carefully investigated by Dr. Reece [23], the Inspector of the Local Government Board, but no definite conclusion was arrived at as to the mode of spread of the infection.

NUMBER OF CASES OF POLIOMYELITIS IN ENGLAND AND WALES FOR THE YEAR 1913.

FIG. 2.—The figures indicate the number of cases of poliomyelitis notified in each county during the year 1913.

(5) *Distribution of Cases of Poliomyelitis in England for the Years 1912, 1913, 1914 and 1915.*

The study of the notified cases of poliomyelitis in England during the years 1912, 1913, 1914 and 1915 shows that the disease is distributed in a very irregular manner (figs. 1 to 4).

NUMBER OF CASES OF POLIOMYELITIS IN ENGLAND AND WALES FOR THE YEAR 1914.

FIG. 3.—The figures indicate the number of cases of poliomyelitis notified in each county during the year 1914.

Lancashire provided the largest number of cases: 192, 83, 80, for 1912, 1913, and 1914, but only 6 in 1915. A marked prevalence in

the same years is to be noted in the contiguous counties of Cheshire, Staffordshire and Warwickshire, and with the same sharp decline in 1915. Northamptonshire, Bedfordshire and Buckinghamshire, severely attacked in 1912, have remained fairly free since.

NUMBER OF CASES OF POLIOMYELITIS IN ENGLAND AND WALES FOR THE YEAR 1915.

FIG. 4.—The figures indicate the number of cases of poliomyelitis notified in each county during the year 1915.

Gloucester had a high incidence in 1915, as had also East Sussex, neither of these counties being severely affected in the previous years.

The study of these maps suggests that poliomyelitis is, in its

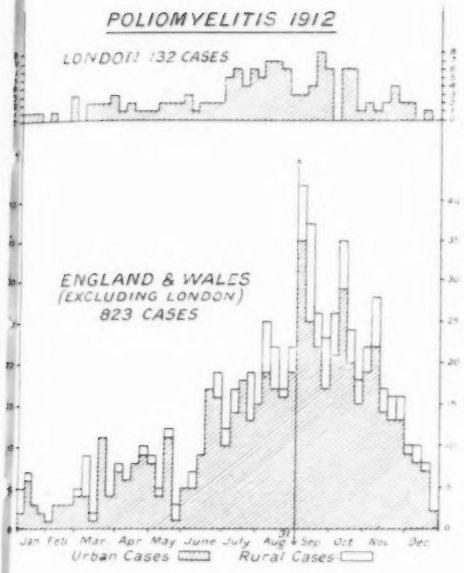


FIG. 5.

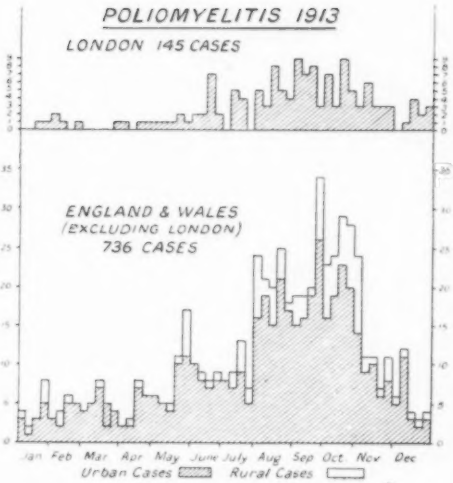


FIG. 6.

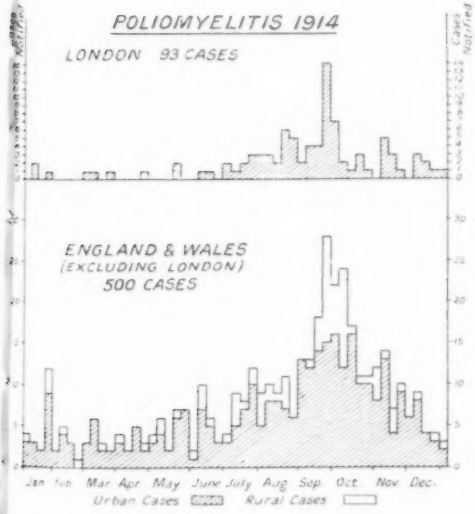


FIG. 7.

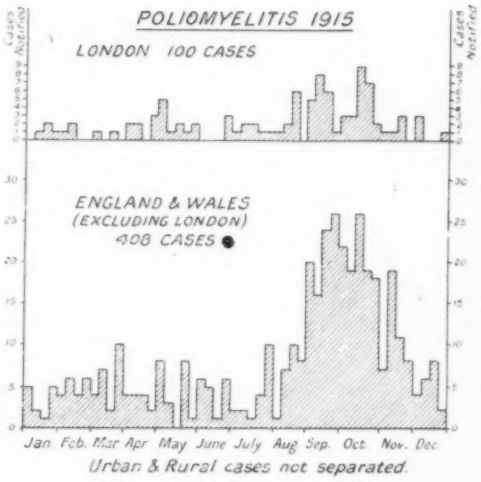

POLIOMYELITIS 1915
LONDON 100 CASES
ENGLAND & WALES
(EXCLUDING LONDON)
408 CASES
Jan. Feb. Mar. Apr. May June July Aug. Sep. Oct. Nov. Dec.
Urban & Rural cases not separated.

FIG. 8.

distribution, similar to meningococcal meningitis, only a very small percentage of the population being affected.

In September, 1911, the Local Government Board, on the recommendation of the College of Physicians, made the disease compulsorily notifiable for London, and in September, 1912, for the whole country.

For the years 1912-13-14-15 some idea can be obtained of the distribution throughout the community. This is indicated on the charts (figs. 5 to 8) kindly supplied to me by Dr. Reece, of the Local Government Board, and on the maps (figs. 1 to 4) compiled from the monthly returns.

During the year 1912, 823 cases of poliomyelitis were investigated by Dr. Reece, of the Local Government Board. The mortality for all ages was 13 per cent.; 51·9 per cent. recovered with permanent paralysis, so that the disease either killed or incapacitated to a greater or less degree 65 per cent. of those who were attacked, leaving a figure of 35 per cent. for complete recovery.

During the year 1913, 736 cases of poliomyelitis were investigated. The mortality for all ages was 14·4 per cent.; 53·6 per cent. recovered with permanent paralysis and 14·4 per cent. died. The disease thus killed or incapacitated in a greater or less degree 68 per cent. of those attacked. These figures would leave a figure of 32 per cent. for complete recovery.

During the year 1914, 500 cases of poliomyelitis were notified. The mortality for all ages was 16·6 per cent.; 47·7 per cent. recovered with permanent paralysis, so that the disease killed or incapacitated in this year to a greater or less degree 64 per cent., leaving a figure of 36 per cent. for complete recovery.

For the year 1915 complete figures are not available; it is known, however, that 408 cases were notified, and their distribution about England is shown in the map. The mortality and incapacity cannot be stated, but the figures for the three years 1912-13-14 having been 65, 68 and 64 respectively, it is unlikely that 1915 would show any great variation.

During the year 1913 an epidemic of poliomyelitis occurred in certain districts in Lancashire and Westmorland. Macewen [19], who investigated the epidemic, says: "It will be observed that the outbreak of poliomyelitis in Barrow was marked by its restriction to young children. The reason for this exceptional incidence of the disease on young children is one of the problems connected with poliomyelitis which still seem to need elucidation."

It is indeed a striking fact that of the nineteen cases specially investigated in Barrow, only two were over the age of 3 years, Nos. 1 and 16, aged 4 and 5 years respectively, occurring in groups 1 and 2 as indicated on the map (fig. 9). Now it is well known that Barrow suffered from a severe epidemic of poliomyelitis, investigated by

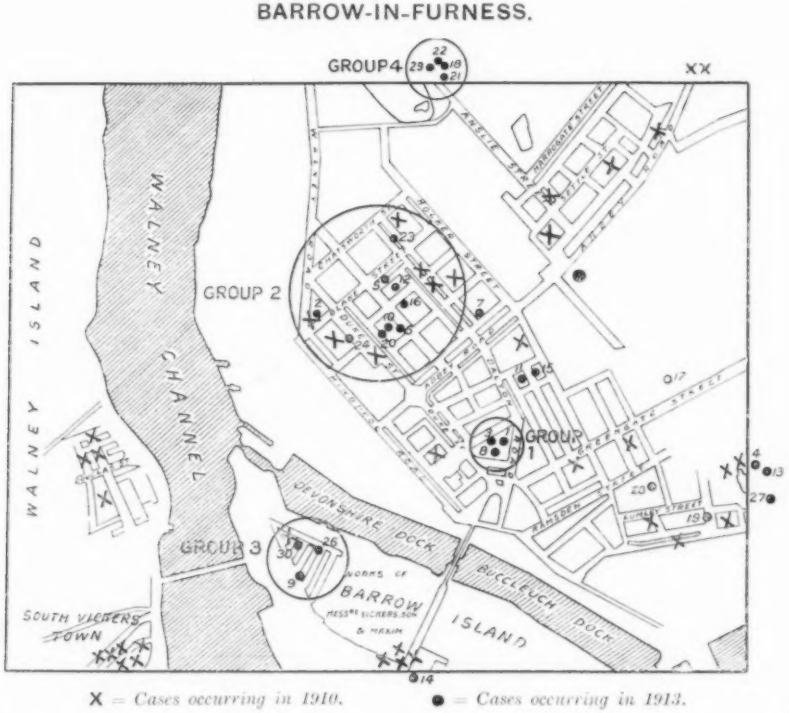


FIG. 9.—Map of Barrow-in-Furness: The x indicates the position of cases which occurred in 1910, investigated by Dr. Garrow; the ● indicate the position of cases occurring in 1913; the numbers, the sequence of the date of onset of the disease: and the circles, groups into which they are arranged by Dr. Macewen.

Garrow [10], in 1910, which left some thirty-seven cripples. So the disease when it occurred again in 1913 fell upon a locality in which the susceptibles had been picked out by the former epidemic, and the population (except for those who had come into existence since 1910) were naturally immune, or had an acquired immunity. It would seem that the susceptible material of a population is fairly soon exhausted. The disease therefore fell on those below the age of 3 years.

It is of interest also to compare Macewen's spot map of the incidence of poliomyelitis in Barrow-in-Furness, 1913, with that of Garrow's in 1910, and notice that the largest group (No. 2) tends to fall into the same area as a considerable number of Garrow's cases. This may be dependent on certain local conditions or may be due to a "virus carrier."

It seems possible that the careful investigation of the various epidemics of this disease will bring to light some causative factor, but it is essential that such investigation should take place at the time of the occurrence of the acute disease and not when the after-effects are the sole record of the epidemic. So far it must be admitted that factor has not been found.

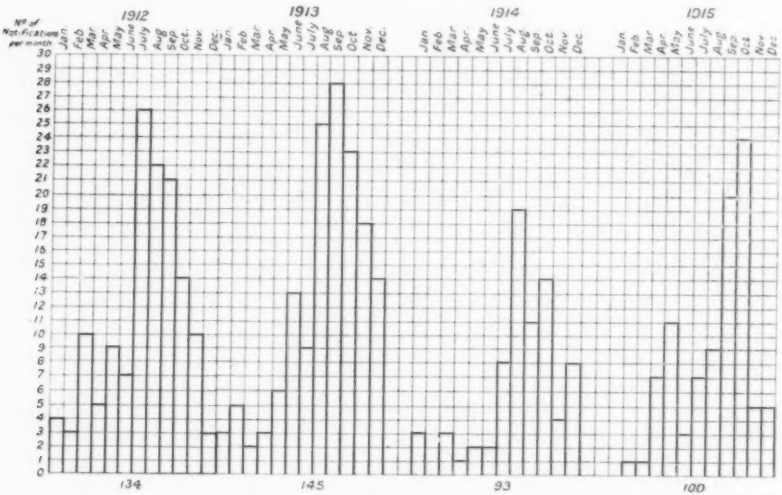


FIG. 10.—Chart showing the monthly returns of cases for years 1912-13-14-15 for the London area. It will be noted that in 1915 the maximum number of cases occurred during October, and not during August and September as in the previous years.

Jubb [15] noted outbreaks of poliomyelitis in West Kirby in three successive years—1912, 1913, 1914—one, seven, and four cases respectively. Roth [24] described a small epidemic in Oxfordshire in 1913, and Pim [22] another small epidemic in Dorset in 1914. Cases were also reported in co. Tyrone in 1914 [13].

The charts prepared from the notified cases of poliomyelitis during the past four years, both in London and the whole of England, show

that the disease has pursued the even tenor of its way with the usual seasonal incidence. There is no reason to believe that its prevalence has been greater or less than it was in years previous to notification. The chart (fig. 10) shows that the prevalence was in London somewhat greater in the year 1913 than in 1914 and 1915. In the year 1915 it is noteworthy that the maximum number of cases occurred not in August, or September, but in October.

(6) *Distribution of Cases in London.*

The study of the distribution of cases in the London area as indicated on the maps (fig. 11) would seem to point to the fact that the districts of Stepney, Islington, Hackney and Wandsworth have an exceptional incidence of the disease.

In 1913, Islington had 19 cases, Hackney 15, Wandsworth 14, and Stepney 14. In 1914, Islington had 8 cases, Wandsworth 2, and Stepney 27. In other districts there is a general evenness of distribution.

In 1914 the exceptional incidence of poliomyelitis which occurred in the East End of London (Stepney, 21 cases; Poplar, 5 cases; Bethnal Green, 5 cases—it will be noted that these figures do not accurately correspond to the notified cases, but the discrepancy is probably due to corrections of the notified returns) was investigated by Brincker [5], but he could determine no common factor. It was noteworthy that eighteen of the thirty-one cases were notified from the London Hospital. The Hospital authorities also observed that during the period when so many cases of poliomyelitis were under treatment a number of other patients were found to be suffering from herpes zoster.

It is quite certain that the number of cases notified does not represent the full extent of the prevalence of the disease in London. It is a well-recognized fact that not a few cases of the disease, when admitted to hospital, have not been notified.

As Dr. Newsholme points out: "Although the disease is under close scrutiny by many observers in different parts of the world, there are many etiological and epidemiological problems associated with it which still require elucidation," and he invites the co-operation of the medical practitioners in attendance on the case and the local medical officer of health.

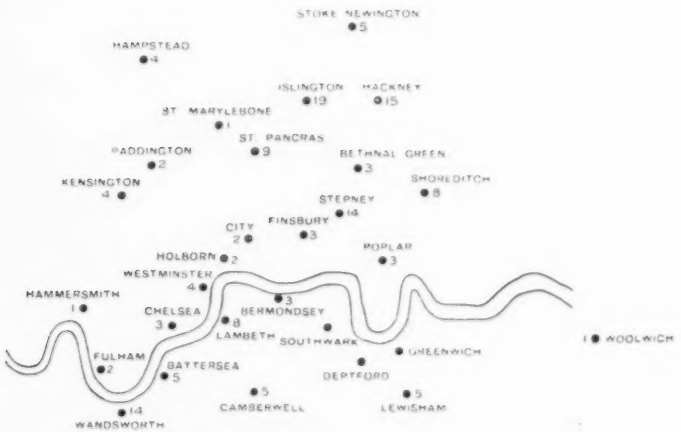
The problem is one which will need a yet larger association of workers, not only the above, but also of those versed in animal

POLIOMYELITIS LONDON 1912. JAN.1 1912 - DEC.31 1912

FROM L.C.C RETURNS 130 CASES NOTIFIED

POLIOMYELITIS LONDON 1913 JAN 1 1913 - DEC.31 1913.

FROM L.C.C RETURNS 145 CASES NOTIFIED



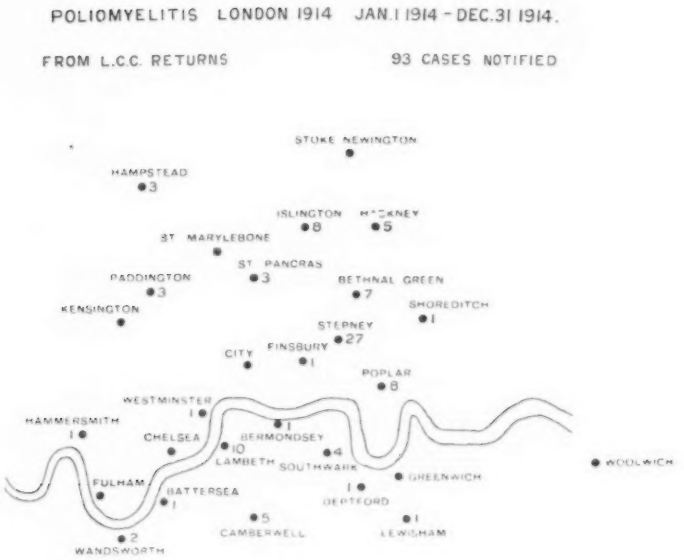


FIG. 11.—A series of maps of the London District for the years 1912-13-14-15, showing the distribution of cases in various areas.

disease, having a knowledge of the method of neurological investigation, both clinical and pathological, and skilled in bacteriological and experimental investigations.

Chapter II.—Pathological Anatomy.

Most observers of the present day regard the essential pathological change which occurs in acute poliomyelitis as an inflammation of the interstitial tissue of the central nervous system. This view has only been arrived at by the careful investigation of numerous observers in every stage of the disease. As methods of preparing and staining tissue improved, so the pathological picture has become more definite, and the views of pathologists as to the nature of the process, which at first were divergent, have become more in accord.

The leading points in the history of the advance of knowledge in this branch of the subject may be briefly stated as follows:—

Heine [38], in 1860, from clinical observation and deductive reasoning, came to the conclusion that the site of the lesion in poliomyelitis must be in the spinal cord.

In 1863 Cornil [35] investigated a case of poliomyelitis of forty-seven years' duration, and found considerable atrophy of the ventro-lateral columns and atrophy of the cells of the anterior horn. He did not, however, attach importance to the latter observation.

Then followed the observations of Prévost and Vulpian (1865) [42], who noted atrophy of the anterior horns and diminution in the number of ganglion cells, as well as atrophy of the anterior and lateral columns. Lockhart Clark (1868) confirmed this observation.

In 1870 Charcot and Joffroy [34] made an examination in a woman, aged 40, who had been paralysed for thirty-three years, and found absence of the ganglion cells, and attributed the atrophy of the muscles to the destruction of these trophic cells. They inferred a primary affection of the ganglion cells, and looked upon the interstitial change as a secondary reaction.

In 1871 Roger and Damaschino [44] demonstrated marked changes in the vessels, with cell proliferation in the anterior horns in more recent cases, and the question of a primary parenchymatous or primarily interstitial process was raised, and left for the time unanswered. Similar observations were published by Charleswood Turner, Frederick Taylor and Drummond in this country.

In 1888 Rissler [43] showed by the examination of acute cases that

the disease consisted in a disseminated infiltration and inflammatory process, which may attack any portion of the central nervous system, but showed a predilection for the grey matter of the spinal cord; but even he contends that the cells are primarily affected and the interstitial changes are secondary. He was the first to show that the pia mater might be involved.

The discussion between primary parenchymatous and primary interstitial process was carried on between numerous observers. Some pointed out the possibility of a simultaneous affection of both the parenchymatous and interstitial elements. The same process was shown to occur in both children and adults.

A series of observers now investigated acute cases, and most of them adopted the interstitial theory. In 1905 Wickman examined a number of acute cases, and in 1910 published further series. He confirmed the work of earlier observers that the process was not limited to the spinal cord, but occurred in a disseminated form in the medulla, pons, cerebrum, cerebellum, and membranes. The variation in the intensity of the process depends upon the varying richness of blood supply to the parts. The process is mainly interstitial and of the infiltrative lymphocytic type. The infiltration follows the distribution of vessels, and inflammatory œdema plays some part. Wickman considers that within the nervous system the inflammation travels along the perivascular lymphatics; the perineural lymphatics probably carry the infection from the site of inoculation to the spinal cord. Since Wickman's pathological investigation numerous workers have carried out observations on acute cases. Harbitz and Scheel consider that the infection is carried to the central nervous system by the blood as well as by the lymph-stream.

Forssner and Sjövall [37] noticed the rôle played by the phagocytes in the destruction not only of the ganglion cells but also in the spinal root ganglia, and Wickman and all recent observers confirm this observation [47].

Farquhar Buzzard, in his Goulstonian Lectures of 1907 [33], discussed the various views which had been advanced to explain the changes observed in the spinal cord. It is unnecessary to repeat these, but his conclusions in the light of recent investigation as to the nature of acute poliomyelitis, based on pathological observations, are of interest, for he says: "It is an acute specific fever occurring sporadically and epidemically; its essential lesion is an inflammation of the interstitial tissue of the central nervous system, due to the presence of micro-organisms, or their toxin, probably in the blood, but possibly in the lymph, circulating within that system."

I have already referred to the very complete observations of recent writers as to the nature of the lesion of poliomyelitis. In dealing with this part of the subject my description will be based mostly on my personal observations of human cases, not that they have been more extensive or complete than those of others, but that they are personal, and therefore more pertinent to these lectures. Endeavour has been made to include all stages and situations of the disease, and where individual observation was lacking, resource has been had to the work of others.

The changes are similar to those found in the experimental disease, *except* such as are described by Kling, Pettersson and Wernstedt [39] under the head "degeneration." Some cases of toxic neuritis show changes similar to those described by these observers, but the proof is lacking that they were cases of poliomyelitis.

Macroscopic Changes.

It may be said that the macroscopic changes observed in the body in a child dying of poliomyelitis are usually slight. Most observers have noted enlargement of the spleen, the thymus and lymphatic glands.

Flexner, Peabody and Draper [36], in 1912, had the opportunity of investigating the organs of ten children who died between the third and eleventh day of illness. Apart from the nervous system upon which the main injury is inflicted, all the cases showed hypertrophy of the lymphoid tissues. The affection of these was widespread, and included the tonsils, small intestine, thymus, and the superficial and deep lymphatic glands. The spleen was enlarged, and the Malpighian bodies prominent. The lesion in the liver consists of hyaline focal necrosis of liver cells, followed by regeneration an invasion by lymphoid cells and polynuclear leucocytes. They consider that the polymorphonuclear-cytosis of epidemic poliomyelitis is caused not only by the lesion of the nervous system, but also by lesions of the lymphatic tissue and liver. This consideration will serve to explain certain discrepancies in the cell counts in the cerebrospinal fluid removed by lumbar puncture and in the circulating blood.

The cerebrospinal fluid is clear, and no change can be noted in the pia mater or pia arachnoid. On one occasion hæmorrhage in the lumbar region was found in an acute case, but it is possible that such was due to the lumbar puncture which had been performed.

The surface of the brain appears in most cases normal, but in one case of encephalitis with hemiplegia there was obvious congestion of the

vessels on the surface. The cord may on palpation, if the disease has been extensive, feel soft, but as a rule no alteration can be noted. In long-standing cases the cord may appear somewhat shrunken, and the grey and atrophied appearance of the ventral roots, as compared with the dorsal roots, is a marked feature. On section through the cord the grey matter, especially in the region of the anterior horn, appears hyperæmic, and in some cases the whole horn may appear filled with blood. Although the hyperæmia chiefly affects the anterior horns, yet it is not limited to this portion of the grey matter. Small dark lines are seen in the white matter, indicating congested vessels, but the white matter generally appears normal.

In cases of long standing, three months or more, the grey matter has a softened and gelatinous appearance, and on section this shrinks away from the level of the section, so that there is a depression in the region of the anterior horn. In the old and long-standing cases the whole cord may be shrunken on one side, and the grey matter especially may appear obviously smaller than that of the other.

In the medulla, pons and brain, areas of congestion similar to those seen in the spinal cord may be observed, and in long-standing cases a cavity may exist in the brain, as shown by White and Worthington [46].

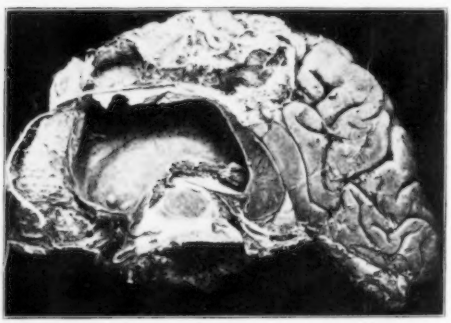
Rossi [45] describes a similar pathological condition in a case of poliomyelitis associated with an encephalitic process in the frontal, paracentral lobule and the corpus callosum. The case was that of a man who died at the age of 40. He had, when 6 months old, convulsions, followed by a paraplegia. The fits never recurred. He did not gain the power of walking. The right leg presented the typical condition of spastic paralysis with flexion of the knee and adduction of the thigh. In the left leg there was an almost complete flaccid paralysis, with wasting of muscles and shortening of the limb. Vasomotor troubles were present, and the reflexes were diminished in the left leg. The pathological examination showed in the cerebral hemisphere a condition of softening to the right and left of the mid-line with dilatation of the anterior portion of the left lateral ventricle. The cord in the lumbar region showed the typical appearance of an old poliomyelitis (figs. 12 and 13).

Microscopic Changes.

These will be described in three stages: (1) the acute, (2) the chronic, (3) the atrophic stage. There is, of course, no hard-and-fast

line of distinction between these stages, but specimens may be taken from cases dying within the first month as illustrative of the acute stage, two or more months after the acute onset as illustrative of the second, and two or more years after acute onset as illustrative of the third stage.

(1) *The acute stage.*—In a certain number of cases the pia mater is found to be infiltrated with small round cells: these cells are generally most numerous around the vessels in the anterior median fissure and



FIGS. 12 and 13.—Photographs of brain and spinal cord, showing a cerebral and a spinal lesion, resulting from poliomyelitis in early life.

Reproduced from the *Nouv. Icon. de la Salpêtrière*. 1907, by the kind permission of Mon. Italo Rossi and Mon. H. Meige.

may be limited to this region (fig. 15). Sometimes the infiltration extends on to the posterior surface of the cord and involves the posterior roots, but often it is limited to the anterior region of the cord.

I do not propose to enter into the discussion as to the nature and origin of these cells, either here or in the spinal cord, but shall be content to designate them lymphocytes or infiltration cells. The whole cytology of the infiltration of the vessel walls, the soft membranes and the grey matter is discussed by Buzzard [33], Wickman [47], Mackintosh and Turnbull [40], Barnes and Miller [28], and Kling, Pettersson and Wernstedt [39]. Buzzard describes five varieties of cells in the infiltration of the grey matter, and says: "Excluding all these cells, there are still a considerable number which it is difficult to classify, and for this reason it is impossible to gauge accurately the relative proportion of the various elements. My general impression is that neuroglial proliferation and lymphocytic infiltration are the most

FIG. 14.—Lumbar region of cord of a child who died on the twenty-eighth day after onset of illness, showing extreme vascular congestion and infiltration of the grey matter most marked in the region of the anterior horns.

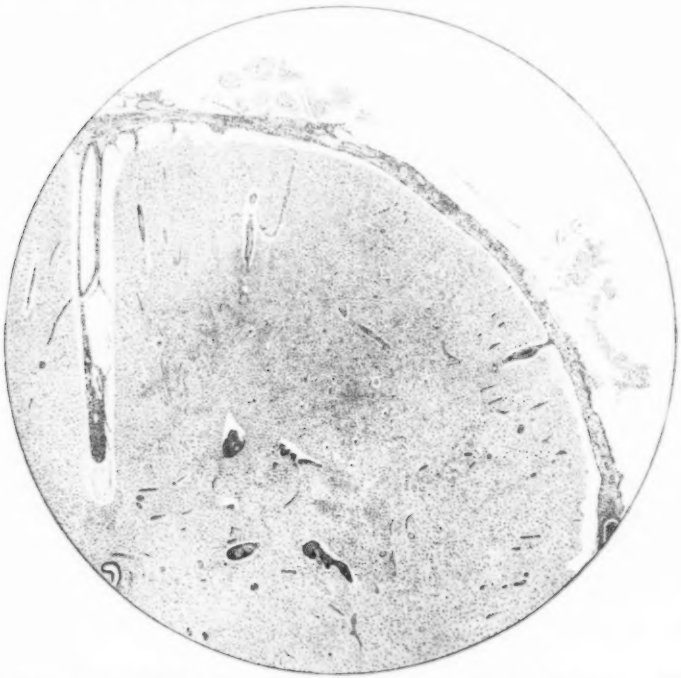


FIG. 15.—Section of spinal cord of a child who died on the ninth day of illness, showing infiltration of the grey matter, perivascular infiltration and invasion of the pia arachnoid membrane. Note that the cells of the anterior horn can still be seen in the infiltrated area.

prominent factors in the production of these cell masses." Mackintosh and Turnbull describe seven varieties of cells.

Spinal cord: The appearance of the spinal cord when stained by the Van Gieson method is very striking (fig. 14): the vessels, and especially those in the anterior median fissure, are dilated and surrounded with small round cells, and the grey matter in the regions of the anterior horns is infiltrated with these cells (fig. 15). The white matter shares to a limited extent in this infiltration, as do also the vessels passing from the pia into the cord, which is in the case figured markedly involved on the anterior surface (fig. 16).

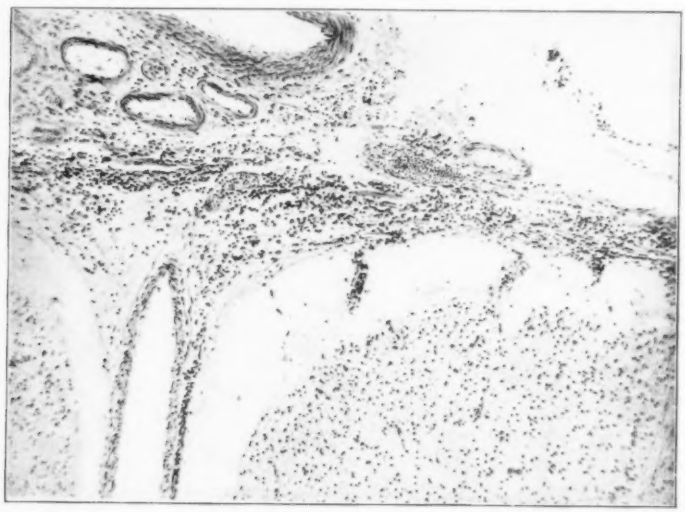


FIG. 16.—Photograph of the same section of spinal cord under high magnification to show small-celled infiltration of the layers of the pia lying next to the spinal cord and the perivascular infiltration of the vessels passing into the cord.

Extravasations of blood, large and small, can be seen in the grey matter, mostly in relation to vessels, both veins and arteries. In later stages of the disease the vessels may appear thrombosed; in the earlier stages there is no evidence of this, though at one time I regarded thrombosis as a cause of the softening [31]. In the grey matter, when the infiltration has not been too extensive, the large cells of the anterior horn can be seen—some of them present a normal appearance, some are surrounded by infiltration cells, and others, again, are being destroyed by phagocytic neuroglia cells (neuronophagia) (fig. 17). Some of the

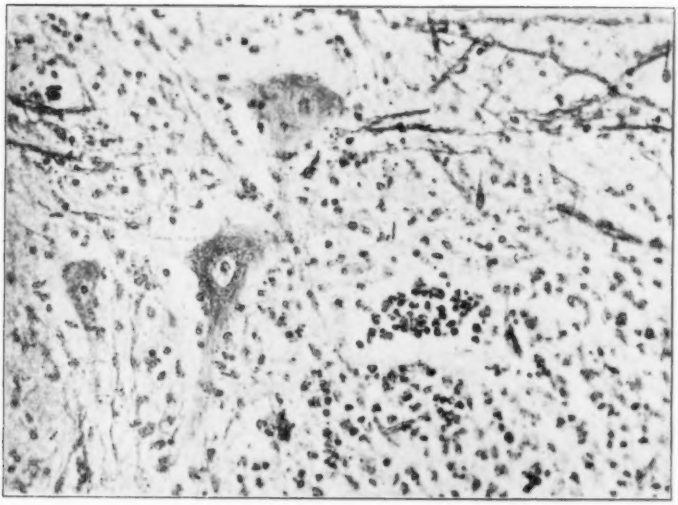


FIG. 17.—Photograph of the ganglion cells of the anterior horn of the same case, showing varying degree of "neuronophagia." Note (i) the cell with a distinct nucleus and nucleolus, with "neuronophagic" cells adherent to the wall, (ii) the cell with indistinct nucleus and "neuronophagic" cells within its substance, and (iii) a cell wholly replaced by "neuronophagic" cells.

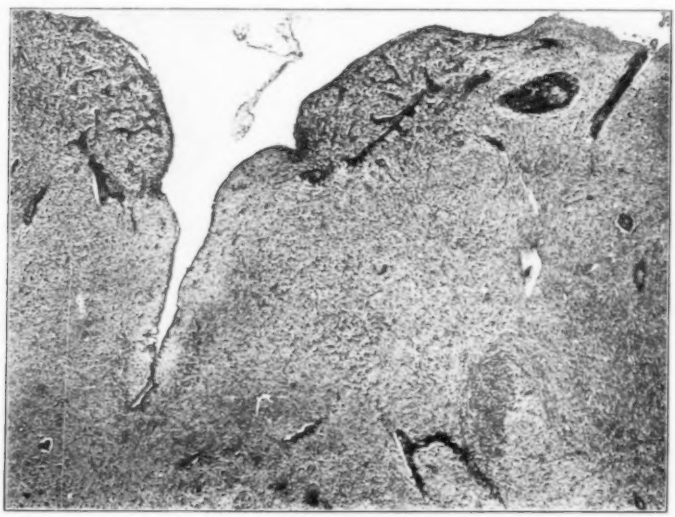


FIG. 18.—Section of medulla and fourth ventricle taken from a child who died forty-eight hours after onset of disease, showing extreme congestion and perivascular infiltrations of vessels and lining membranes of the fourth ventricle; there was also extensive poliomyelitis of the spinal cord.

ganglion cells are entirely replaced by neurophagic cells. Portions of the grey matter other than the anterior horns may be affected, and the changes are similar.

The posterior root ganglia show the same cellular infiltration and cytological changes. Flexner states that experimentally lesions of the ganglia are as common and constant as the lesion of the grey matter, and in man are probably as constant, but not so frequently looked for.

FIG. 19.—Section of spinal cord of a child who died six weeks after the onset of the disease, stained by Marchi method, showing degeneration of the efferent fibres of the anterior roots.

In the medulla and mid-brain changes similar to those in the spinal cord can be observed, and these are present in cases which, during life, have exhibited no marked bulbar or pontine symptoms. In the specimen shown (fig. 18) the poliomyelitic changes are most marked in the region of the fourth ventricle and invade the lining membranes of that cavity. The boy from whom this specimen was taken rapidly passed into coma and died in forty-eight hours.

One interesting case of facial paralysis on one side is on record in which the seventh nerve nucleus on that side was destroyed, while that on the opposite side was unaffected [30].

(2) *Chronic stage.*—The study of the changes in the spinal cord

during the chronic stages is of considerable interest. They show the local destructive lesion giving rise to necrosis, to secondary degeneration taking place in the efferent portions of the anterior root, and to degeneration of antero-lateral tracts in the spinal cord resulting from these lesions (fig. 19). In general, the lesion is too diffuse to be of much service for tracing the endogenous fibres of the cord, but Mott [41] has

FIGS. 20, 21, 22.—A series of three sections taken from the lumbar cord of a child who died seven weeks after the onset of the disease: (i) stained by Marchi method; (ii) by Weigert Pal method; and (iii) by Van Gieson method.

FIG. 20.—Gives a positive picture, the degenerated myelin and the fat in the cells in the perivascular space being stained black.

been able to trace such in one case, and Holmes and myself [32] were able to trace the intra-medullary course of the spinal portion of the spinal accessory nerves in another.

During this stage the changes are best shown by the Marchi and Weigert-Pal method. The Marchi stains the degenerate myelin tissue black, whilst the Weigert-Pal stains the normal fibres a dark blue. Positive and negative pictures are therefore presented respectively.

Fig. 20 represents a section through the lumbar region of the cord and shows an area of necrosis, limited to the external portion of the anterior horn. The vessels are stained black, owing to the loading of the perivascular lymphatics with the products of degenerated myelin. In the antero-lateral tract of the spinal cord numerous black dots can be seen, representing degenerated fibres.

Fig. 21.—Gives a negative picture, the area of complete degeneration being white—the number of the medullated fibres in the grey matter of the anterior horn is diminished.

If this positive picture is compared with the negative picture presented by the Weigert-Pal method (fig. 21), it is clear that the destruction of tissue is widespread, and in some directions more extensive than that presented by the positive picture. The myelin sheaths have been destroyed for a considerable distance beyond the necrotic area, so that practically the whole of the anterior horn is involved, though not to the complete extent to which the external portion has suffered. The products of degeneration have to a considerable extent been removed from the peripheral portions of the lesion.

The specimen stained by hæmatoxylin (fig. 22) shows the remains of the inflammatory process and the formation of new tissue.

(3) *Atrophic stage* (two years or more).—In the *atrophic stage* the products of necrosis become absorbed—the anterior horns undergo shrinking, and the whole of the grey matter on the affected side becomes atrophied. The white matter also suffers, but relatively less than the

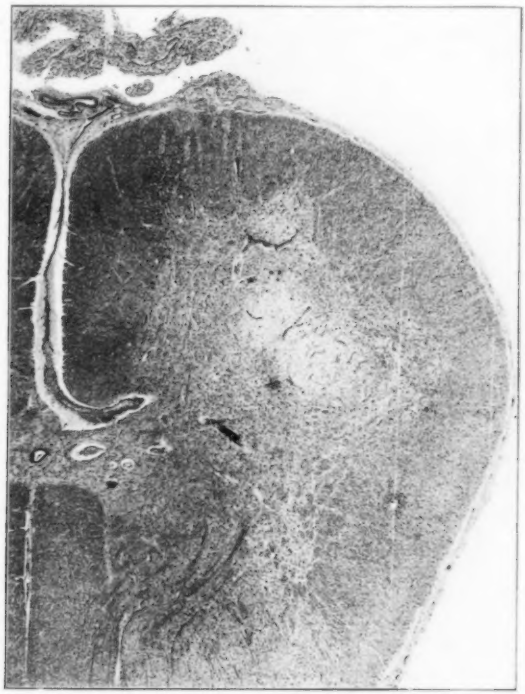


FIG. 22.—Gives a positive picture, the glia tissue with but few cellular elements taking the place of the degenerated tissue.

grey matter, and the whole of the anterior lateral tracts of the cord are pale and diminished in size, and in some cases a sclerotic area is left in the anterior horn (fig. 13).

Peripheral nerves: In the acute stage, cell infiltration can be found in the peripheral nerves (fig. 23), but it is difficult to say that such infiltration produces any symptom or pathological effect. The observations on the point are not extensive, and need further investigation. The

specimen (fig. 23) is taken from the anterior crural nerves of a boy, aged 5, who died on the ninth day after the onset of acute poliomyelitis. In long-standing cases the Marchi method shows the usual degeneration of the efferent fibres. The Weigert-Pal method shows that the number of normal fibres left in a degenerated nerve is very considerable: such fibres are usually of large size, and are probably largely afferent in function. No true interstitial change can be found in the nerves.

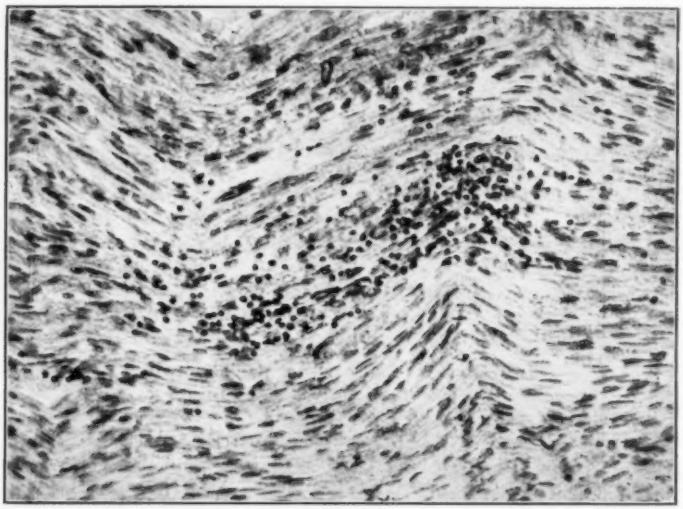


FIG. 23.—Longitudinal section of anterior crural nerve of a boy who died on the ninth day of the disease. The specimen shows round-celled infiltration of the nerve.

Muscles: The study of the muscle in the chronic and late stages of the disease is of interest. A muscle which is not wholly degenerated shows normal muscle-fibre alongside with fibres and bundles of fibres which have undergone complete degeneration and been replaced by fibrous tissue. In those cases in which the muscles have undergone complete fibrous or fatty degeneration, it is interesting to note that the muscle-spindles still exist [29], and contain a normal and well-striated muscle-fibre and a normal nerve. It is a striking fact that certain muscles seem to undergo a fibrous degeneration, whilst others undergo a fatty degeneration. As an instance of this former may be mentioned the biceps, as an instance of the latter the gastrocnemius.

In concluding this review of the pathology of the subject, it may be

said that so far as our present knowledge goes the pathological picture above presented is (with the exception of rabies) distinctive of the virus of poliomyelitis.

Chapter III.—Experimental Poliomyelitis.

(1) *Earlier Experimental Work.*

In 1909 Landsteiner and Popper succeeded in transmitting poliomyelitis to two monkeys, but failed to propagate the experimental disease beyond the first generation. In the same year Knöpfelmacher and Strauss and Huntoon in America were also successful in producing the disease in monkeys by injecting into the peritoneum an emulsion of the spinal cord from cases of poliomyelitis.

Flexner and Lewis, in 1910, overcame the difficulty of propagation by substituting intra-cerebral for intra-peritoneal injection, and were the first observers to transmit the disease through a series of monkeys. As Flexner points out, the choice of an intra-cerebral route as superior to the intra-peritoneal route was not haphazard, as all the severe effects of poliomyelitis are inflicted on the nervous system, and, upon reflection, this fact at once suggested that the parasitic cause of the disease must find favourable conditions for multiplication within the nervous tissues [49].

Landsteiner and Levaditi showed that the virus would pass through porcelain filters and also that glycerine did not destroy it. Working on the same lines and at the same time, Leiner and Wiesner in Vienna, Roemer and Joseph in Marburg, Krause and Meinicke, confirmed these observations and added much to the knowledge of the nature of the virus [48], [50].

(2) *Properties of the Virus.*

(*a*) *Filterability.*—It was shown by Flexner and Lewis and Landsteiner and Levaditi that the virus would pass through a porcelain filter. The latter observers noted that it would pass through the Berkefeld, Chamberland, Reichel and Pukall filters, but that, after such a passage, the virus lost some of its virulence, and the incubation period was always prolonged, and the monkey either did not die or only died some days after the development of the disease.

(*b*) *Glycerine resistance.*—It has been shown by Landsteiner and Levaditi that the virus will resist the action of glycerine either concentrated or with 50 per cent. of water without impairing its

virulence. The virus has been kept by Flexner for twenty-five months in glycerine at a temperature of 4° C. without affecting its virulence. In this respect it resembles that of rabies and vaccinia.

(*c*) *Resistance to drying.*—Flexner and Lewis, Landsteiner and Levaditi, found that prolonged drying, even for twenty-four days, at a temperature of 22° C. did not diminish the virulence, so that in this respect it differed from rabies. Leiner and Wiesner, however, found that drying of thin films for four hours at a temperature of 37° C. did destroy the virulence. They showed that the virus is killed by exposure to a temperature of 55° C. for half an hour, and it is not killed by exposure to a temperature of −8° C. Flexner found that long exposure (eighteen to thirty-six months) to a temperature of −2° C. to −4° C. did destroy the virulence of the virus.

(*d*) *Resistance to disinfectants.*—It has been shown by Landsteiner and Levaditi that 0·2 per cent. solution of potassium permanganate will kill the virus in one hour at a temperature of 39° C., and that 6 per cent. peroxide at the same temperature will destroy the virus in forty-five minutes. The virus is not killed by ½ to 1½ per cent. of carbolic acid.

(3) *Cultivation of the Organism.*

In October, 1913, Flexner and Noguchi [59] published the method by which they had succeeded in cultivating the organism of poliomyelitis under anaerobic conditions in ascitic fluid to which fresh rabbit's kidney has been added.

The micro-organism consists of globoid bodies measuring from 0·15 μ to 0·3 μ in diameter, and arranged in pairs, chains and masses, according to the condition of growth and multiplication. The chain formation takes place in a fluid medium, the other grouping in both solid and fluid media. Within the tissues of infected human being and animal, the chains do not appear. Whether the micro-organism actually belongs to the bacteria or to the protozoa has not been determined, but it is pointed out that the organism is associated with the production of an acute disease in which suppuration does not form a prominent part.

The experimental disease caused by the inoculation of cultures resembles that produced by the virus of poliomyelitis as ordinarily employed. The cultivated micro-organism withstands the action of glycerine, passes through the Berkefeld filter, and the filtrates yield, upon recultivation, the particular organism contained within the filtered culture. By employing suitable staining methods the micro-organism

can be detected in film preparations and in sections of nervous tissue from monkeys infected with cultures. The organism thus fulfils the condition hitherto demanded for the establishment of causal relations between an extraneous parasite and a specific disease: The micro-organism exists in the infectious and diseased organs; it is not, so far as is known, a common saprophyte or associated with any other pathological condition; it is capable of reproducing on inoculation the experimental disease in monkeys, from which animals it can be recovered in pure culture. Besides these classical requirements, the micro-organism withstands preservation and glycerination, as does the ordinary virus of poliomyelitis within the nervous organs.

Flexner and Noguchi, in conjunction with Amoss [51], [60], have now continued their investigation of the organism further, and having carried the strain through twenty subcultures have proved that the final culture was pathogenic to monkeys.

The micro-organism isolated from poliomyelitic tissues may possess pathogenic properties after having been cultivated artificially for a period of a year or more, and after an almost indefinite degree of dilution of original nervous tissues from which it was derived.

The micro-organism cultivated from poliomyelitic tissue is adapted with difficulty to saprophytic conditions of multiplication, but once adapted growth readily takes place upon suitable media. When, however, as a result of inoculation into monkeys the parasitic propensities of the micro-organism are restored, it again displays the same marked fastidiousness to artificial conditions of multiplication present at the the original isolation.

Flexner, Noguchi, and Amoss end their paper with the following guarded conclusions:—

That the experiments afford additional strong evidence in support of the view already expressed that the micro-organism bears an etiological relationship to epidemic poliomyelitis in the human subject, and to experimental poliomyelitis in the monkey.

(4) *Method of Infection.*

The emulsion is prepared by pounding up 1 grm. of the infected portion of the spinal cord with 20 c.c. of normal saline solution; 0·5 c.c. of this emulsion is injected into the brain and 4 c.c. to 5 c.c. into the peritoneal cavity (Roemer). The amount of virus required is extremely small—viz., less than $\frac{1}{1000}$ c.c. of a 2·5 suspension of spinal cord.

The most certain method of producing infection is by injection of

the virus into the brain. Injection into the peritoneal cavity, the anterior chamber of the eye, the subcutaneous tissue, intraspinal, intraneural, and intravenous injections have all been successful in producing the disease.

It has been shown (Flexner and Lewis, Levaditi and Landsteiner) that the virus injected into a peripheral nerve gives rise to paralysis, the disease commencing in the limb corresponding to the nerve injected.

Leiner and Wiesner found that if the nerve is divided immediately after the introduction of the virus into the peripheral end, the spread of the disease is prevented. In whatever way the animal is infected it is in the central nervous system, and especially the grey matter of the cord, that the virus tends to locate itself.

Leiner and Wiesner showed that the virus could pass through the gastro-intestinal mucosa, but other observers, Levaditi and Landsteiner, failed to obtain positive results, and suggest that infection only takes place if there is a previous lesion of the intestinal walls. Leiner and Wiesner, in order to avoid the action of gastric juice, injected the virus into certain portions of the intestines after opening the abdomen. Three of the four monkeys thus operated on developed poliomyelitis. Flexner, Clarke and Dochez showed [57] that the virus could survive the action of both the gastric and intestinal secretions.

The virus will pass the nasal mucous membrane if injured (Landsteiner and Levaditi), but Leiner and Wiesner have shown that it will pass the uninjured mucous membrane. Natural contagion has been reported in a monkey which was kept in a cage in which the virus had been smeared over the bars; non-infected monkeys have been kept in close contact in the same cage with infected monkeys without contracting the disease (Levaditi and Danulesco [65]).

The great epidemic of poliomyelitis in Sweden, in 1911, gave the observers Kling, Pettersson, and Wernstedt [64] the opportunity of an investigation on somewhat different lines from those previously adopted. They obtained washings from the mouth, nose, pharynx, upper air-passages, and small intestine of a number of patients—(1) dead of the disease; (2) living cases; (3) abortive cases; (4) healthy persons in contact with infected individuals. Washings from these mucous membranes were filtered through a Heims asbestos filter, and by a combined intraperitoneal injection with an inoculation into one sciatic nerve of the filtrate they succeeded in infecting monkeys.

(1) *Dead of the disease.*—Out of fourteen patients dead of poliomyelitis thus investigated, in only one were the authors unsuccessful in demonstrating the presence of the virus of poliomyelitis.

It is, however, interesting to note that the changes in the spinal cord, which have been considered most characteristic of poliomyelitis —i.e., cellular infiltrations—were not always present. In fact, out of fifty-nine monkeys which were infected from typical cases of poliomyelitis, twenty-five—i.e., 42 per cent.—showed infiltrative changes, and thirty-four—i.e., 58 per cent.—degenerative changes.

(2) *Living cases of poliomyelitis.*—Having obtained results from persons dead of poliomyelitis, the authors next proceeded to investigate the secretions from living persons, and they obtained material from the mouth, nose, pharynx, and large intestine of twelve living persons suffering from poliomyelitis. In only one case did the observers fail to infect the monkeys.

Thus the presence of the microbe has been detected in the secretions of one of the examined membranes—i.e., mouth, nose, upper air-passage, or intestine—in twenty-four out of twenty-six cases.

Considering the difficulty of infecting monkeys in every instance, the observers consider themselves fully justified in drawing the following conclusion, viz., that the virus in all probability is always present in the mucous membranes of the nose, mouth, pharynx, and the intestine of persons affected by poliomyelitis during the acute stage of the disease.

(3) *Abortive cases, and* (4) *healthy persons in contact with infected individuals.* — Having obtained results from persons suffering with definite poliomyelitis, the authors proceeded to investigate the washings from the mucous membranes of abortive cases and healthy persons. In a family of five, one of whom had definite poliomyelitis, two an uncertain illness of short duration, and two had remained well, they showed that three carried the microbe of poliomyelitis in their mucous membranes—viz., the one who had distinct paresis, one of those who had had an abortive attack and one of those who had had no illness.

The existence of the micro-organism of poliomyelitis has been demonstrated also in the secretion from the mouths of three persons who had not, as far as is known, had any contact with patients showing definite paresis, persons whose illness was characterized by such vague symptoms that only in one case did the suspicion arise that some form of poliomyelitis was present.

In six families the experimental method has demonstrated the existence of carriers of the virus in several members of the family, only one person in each family having typical paralysis. It is therefore probable that virus carriers are very common.

Flexner, Clark and Frazer [58], dealing with passive human

carriage of the virus, demonstrated its presence in the throats of the parents of a child suffering with the disease and confirm in this respect the above observations.

Intraspinous infection.—So far no one has detected the virus in the cerebrospinal fluid in human cases of poliomyelitis, and it is usually absent in the spinal fluid of monkeys at the time of the onset of paralysis, although it may be present at an earlier period after intracerebral inoculation.

Flexner, and Clark and Amoss [52] [54], carried out a series of experiments of infecting monkeys by the method of intraspinous injection of the virus. They experienced no great difficulty in securing infection by this route, although somewhat larger doses of an active virus were required. The virus could be demonstrated in the sub-arachnoid spaces for forty-eight hours after injection, but it was no longer present on the sixth day, at the time when the first symptoms of infection had made their appearance. The failure of the cerebrospinal fluid from human and experimental cases of poliomyelitis to produce the disease when inoculated into monkeys is due to the fact that the virus is either fixed by the nervous tissue or has passed into the blood, which tends to destroy it.

Propagation of the virus by the blood-stream.—It is recognized that the intravenous method of inoculation, even when such large quantities as 50 c.c. to 100 c.c. of the virus are used, is an uncertain and inconstant method of producing infection, although so small an amount as 0·5 c.c. of the same virus succeeds when introduced into the brain. It has also been shown that when infection does occur the incubation period is greatly delayed, in one instance to nineteen days, and during this period the cerebrospinal fluid contained the organism [53].

Flexner and Amoss [54] have made a careful study of this point, and by a series of experiments they trace this discrepancy to the apparent inability of the virus to enter directly the substance of the brain and spinal cord from the blood.

In order to reach these organs the virus must leave the blood and pass into the cerebrospinal fluid, and this it can only do if the choroid plexuses are rendered unduly penetrable, either by excessive doses of the virus or by aseptic inflammation produced by the injection of horse serum.

In the passage of the virus through the cerebrospinal fluid they have shown that it is possible to prevent infection by the injection of an immune serum in the sub-arachnoid space by lumbar puncture. The

virus when injected into the blood is deposited promptly in the spleen and bone-marrow, but not in the kidney, spinal cord, or brain, but the inter-vertebral ganglia remove the virus from the blood earlier than does the spinal cord or brain. They believe that these experiments support the view that the infection in epidemic poliomyelitis in man is local and neural and by way of the lymphatics, and not general by way of the blood; hence they uphold the belief that the entrance is from the upper respiratory mucous membrane.

Incubation period.—The incubation period is subject to very considerable variations. The variations depend upon—(1) The method of injection; (2) the amount of virus given; and (3) the method of treating the virus before injection. Of eighty-one monkeys infected by Lewis and Flexner, forty-seven became paralysed between the eighth and the twelfth day, eighteen became paralysed before the eighth day, and sixteen after the twelfth day. Levaditi found the average incubation period from seven to ten days, and Roemer gives the incubation period as nine days.

In Kling, Pettersson and Wernstedt's series, although the incubation varies within very wide limits, yet the average duration works out at nine to ten days.

The following factors were found to govern the incubation period: The less virulent the material, the longer was the incubation period. Filtration diminished the virulence (Levaditi and Landsteiner, Leiner and Wiesner). Thus an unfiltered emulsion produced poliomyelitis in seven days; the same quantity of filtered emulsion produced poliomyelitis in twenty-seven days.

The quantity given also alters the incubation period. Dilution, again, has the same effect, and if diluted beyond a certain limit the virus will not produce poliomyelitis (Roemer). Thus an animal, injected intra-cerebrally with 0·5 c.c. of a 5 per cent. spinal cord emulsion, became paralysed on the seventh day and died on the eighth day. Another monkey, inoculated with the same quantity but ten times less concentrated, became ill on the twelfth and died on the thirteenth day. Another monkey, injected with the same quantity 100 times diluted, survived without having manifested any paralytic symptoms.

Leiner and Wiesner found that inoculation of a very concentrated virulent emulsion appeared to exercise rather an unfavourable influence on the development of poliomyelitis. The incubation period was slightly longer and the course of the disease goes on as if in the nervous tissues there were, in addition to the acting virus, certain preventive substances which exercised a neutralizing action on the virus.

What happens during the incubation period? Leiner and Wiesner showed that the virus spread to the nervous system before it was possible to observe any morbid manifestation in the central nervous system. Levaditi and Landsteiner found that the anatomical and pathological alterations commenced at a time very close to the outbreak of clinical signs. The virus of poliomyelitis can invade the nervous system and multiply there without causing for a time any apparent trouble or distinct lesion. The paralytic phenomena in a monkey may commence very suddenly—i.e., the monkey may be quite well in the morning and completely paralysed by the evening. It is a striking fact that in the majority of cases, in spite of the inoculation of the virus into the brain, the disease commences by paralysis localized to the lower extremities.

(5) *Immunity.*

On clinical grounds there is good reason to believe that an individual who has survived an attack of poliomyelitis is immune to a second attack. Experimentally it has been shown by Flexner and Lewis, Levaditi and Landsteiner, and Roemer that monkeys which have survived the acute period of infection are immune to a fresh dose of the virus. Roemer considers that immunity is only acquired after about the twenty-fourth day, but other observers do not confirm this observation.

In one case Leiner and Wiesner have been able to reinfect a monkey which was paralysed for eighteen days. This is probably an exceptional instance. Leiner and Wiesner performed experiments to determine if the nervous system of monkeys, killed after the acute state had passed and the refractory stage reached, contained an appreciable quantity of active virus. They found that they could transmit the disease by using the spinal cord of a monkey killed on the twenty-fourth day of the disease. This would seem to show that the active virus and the antibodies can exist at the same time and in the same individual.

Production of artificial immunity.—Levaditi and Landsteiner used the same method for rendering a monkey immune against poliomyelitis as is used for producing immunity against rabies. To a certain extent this method was successful, but in some cases poliomyelitis has been produced by injection of the dried cords. Flexner and Lewis, by giving injections of diluted virus, were able to make monkeys immune to many times the lethal dose.

After recovery from poliomyelitis, both natural and experimental, it has been shown that an active immunity has developed. The state

of immunity is associated with the occurrence in the blood of principles that neutralize the virus. Netter and Levaditi showed this in human cases [68].

Flexner, Clark and Amoss [56] carried out a series of experiments to determine whether antibodies existed within the cerebrospinal fluid. It is known that antibodies are not secreted in appreciable quantities in the cerebrospinal fluid. The experiments show that the cerebrospinal fluid of convalescents tends to be devoid of the neutralizing immunity principles for the virus of poliomyelitis, although they may exceptionally be present within the fluid.

(6) *Experimental Investigations with the Object of Determining the Possibility of Transmission of Poliomyelitis by Means of Dead Objects and Flies.*

Flexner and Lewis, Landsteiner and Levaditi and Roemer found that prolonged drying, even for twenty-four days at a temperature of 22° C., did not diminish the virulence of the virus. Leiner and Wiesner, however, found that drying of the film for four hours at a temperature of 37° C. did destroy the virus. Landsteiner, Levaditi, and Pastia found that the virus remained potent in sterile milk and sterile water for at least thirty-one days.

Josefson succeeded in producing experimental poliomyelitis with a handkerchief and fancy work which had been in contact with a patient suffering from poliomyelitis. Neustaedter and Thro succeeded, after many failures, in producing poliomyelitis in a monkey with a filtrate of macerated dust collected from rooms in which cases of poliomyelitis had been nursed.

Howard and Clark [62] showed that the domestic fly can carry the virus of poliomyelitis in an active state for several days upon the surface of the body, and for several hours within the gastro-intestinal tract, and that the bed-bug has taken the virus with the blood from infected monkeys and maintained it in a living state within the body for a period of seven days.

Lice have not taken the virus out of the blood of monkeys or maintained it in a living state. Kling, Pettersson, and Wernstedt failed to communicate the disease by the means of fleas.

Rosenau, in 1912, demonstrated that poliomyelitis could be transmitted from monkey to monkey by the means of the bite of the stable-fly (*Stomoxys calcitrans*), and this observation has been confirmed by Anderson and Frost. These experiments are the more remarkable,

for it is a matter of some difficulty to infect a monkey with the blood of a patient suffering from poliomyelitis, and as a rule a considerable quantity is required.

Clark, Fraser and Amoss [53], in 1914, conducted a further series of experiments with Stomoxys which gave wholly negative results, and a second series conducted by Anderson and Frost were similarly negative, as were also those of Sawyers and Herms.

Francis [61] made an attempt to transmit poliomyelitis by the bite of *Lyperosia irritans* (a blood-sucking fly), but the experiments yielded entirely negative results.

The whole of the experimental evidence is strongly against the communication of the disease to man by the means of fleas, lice, bugs, and flies.

(7) *Variation in the Pathogenicity of the Virus.*

Flexner and Clark state that they have succeeded in implanting upon monkeys all ten strains of human virus which they examined. That is to say, monkeys have been infected from ten human cases. These authors state that other experimenters have only been able to implant about one-half of the human strains of poliomyelitic virus upon monkeys. In order to succeed in all instances, it is necessary to inoculate emulsions of the human spinal cord, and preferably to make double inoculation into the brain and peritoneal cavity.

English strains have only twice been implanted on monkeys: (1) Levaditi [66] in Paris, with material supplied to him by Gordon from the Cornish epidemic in 1911, succeeded in reproducing the disease from the spinal cords of three cases out of four sent to him; (2) McIntosh and Turnbull [67] in 1913 succeeded in two out of four cases from the London Hospital.

The human strains of the virus not only infect monkeys less readily than do the modified or monkey strains, but the experimental disease produced by them is less severe and less fatal. After the strains have once become wholly adapted to the monkey the paralytic disease appears in a more severe form and the degree of infectivity rises, so that exceedingly minute doses of a filtrate are capable of producing constant infection.

Flexner says the Swedish virus of 1911 appears to be the most powerful yet studied; this is indicated by the fact that saline washing of the nose, throat and intestine could be inoculated successfully after removal of all bacteria by filtration, in nearly every instance.

In America it has been difficult to procure infection with these materials, from which it has been concluded that the virus displays degrees of infectiveness to monkeys. This is further borne out by the difficulty of transmitting the sporadic English cases, as shown by McIntosh and Turnbull.

Natural Variation in the Pathogenicity of the Virus.

Flexner, Clark and Amoss [56] found that a strain of poliomyelitic virus propagated in monkeys for four years displayed during that time three distinct phases of virulence. At the outset the virulence was low, but by animal passage it quickly rose to a maximum; the maximum was maintained for about three years, when without known changes in the external conditions a diminution set in and increased until at the expiration of a few months the degree of virulence about equalled that present at the beginning of the passage in monkeys.

By resorting to the original specimen from which the virus was obtained a highly virulent strain was again produced. It is clear, then, that the frequent and long-continued passage through monkeys finally brings about a depression of virulence, whilst preservation in a state of latency for a period equally great exerts no depressing action.

The cycle of changes in virulence is correlated with the wave-like fluctuations in epidemics of diseases, which also consist of a rise, temporary maximum, and fall in the number of cases produced.

It is this variation in the epidemic which has led to the formulation of the hypothesis of concomitant causes of von Pettenkofer and of Nägeli.

Whilst the one supposes a necessary ripening of the microbic agent in the earth as a pre-requisite, the other invokes the co-operation of a second, although unknown but subsidiary, micro-organism. In these experiments of Flexner, Clark and Amoss we have an explanation of the wave of epidemic disease due to variation in the quality of the virulence of the micro-organism causing the disease.

(8) *The Clinical Picture of Experimental Poliomyelitis in Monkeys.*

The clinical picture of experimental poliomyelitis in monkeys as described by Landsteiner and Levaditi, Flexner and Lewis, and others is similar to that which occurs in man. In addition to the ordinary type of limb paralysis, the muscles of the face, the oculo-motor muscles may be paralysed, sometimes alone, sometimes in association with limb

paralysis, and Roemer has reproduced the "jump" type in monkeys, and relapses occur as a rare manifestation as in man. In view, however, of the pathological finding of Kling, Pettersson and Wernstedt [64], who stated that a considerable number of their cases showed degenerative changes, it is important to study the clinical picture in their cases. That the clinical picture of experimental poliomyelitis may vary is shown by Leiner and von Wiesner, who have described a type of slowly progressive weakness in monkeys which they have designated as "marasmic."

Kling, Pettersson, and Wernstedt have divided the 116 monkeys who suffered from poliomyelitis into six clinical groups: (1) an upper limb, (2) a lower limb, (3) a mixed, (4) cerebral and bulbar type, (5) general muscular weakness, (6) "found dead." The first four groups are so well known and correspond to the usual type in man that no comment is necessary (except that in only one monkey did the illness commence with cerebral symptoms). With regard to the "general muscular weakness" which the authors use as synonymous with the "marasmic type" of Leiner and von Wiesner, it has no known counterpart as a clinical type in man.

The feature of this "general muscular weakness" group is weakness without localized paresis, and the authors state that they have found the disease manifesting itself in this manner in no fewer than twenty-six out of the 116 cases.

A monkey (No. 140) inoculated on November 1 was noticed on November 16 to be more slow in its movements. By November 20 it moved somewhat joltingly, but was otherwise well, possibly weak in the fore-limbs on November 25. It has during the past days been huddled up in one spot, and to-day is lying at the bottom of the cage and moves very little. It died on this evening.

Microscopical examination showed marked hyperæmia and hæmorrhages, but no cellular infiltration. Some of the glia cells distinctly enlarged. The ganglion cells generally dark and rather homogeneous, some of them being besides shrunken and vacuolated, enlarged glia cells often having eaten their way into them; the changes, however, on the whole, not very pronounced.

The clinical picture differs considerably from that which is usually accepted as that of poliomyelitis, as do also the pathological findings. The question might well be asked, Is this disease poliomyelitis?

Flexner, Clark and Fraser [58] are unwilling to accept these pathological findings as evidence of poliomyelitis because similar lesions have

not been shown to be present in fatal cases of poliomyelitis in man and because the organs of monkeys showing such lesions were only occasionally reinoculable and did not cause in the second generation in monkeys characteristic histological effects.

(9) *Pathological Changes found in Experimental Poliomyelitis.*

Most observers agree that the histological changes characteristic of epidemic poliomyelitis are similar in man and monkey. The lesions consist of necrosis and degeneration of the ganglionic nerve cells, with œdema, hæmorrhage, and leucocytic infiltration of the ground substance, the sheaths of the blood-vessels and the membranes.

Wickman believes that the virus produces both interstitial and parenchymatous lesions; Leiner and Wiesner think the virus attacks the parenchyma of the nervous system primarily, and the interstitial changes are secondary.

Flexner, from his histological study of spinal cords in the pre-paralytic stage of the experimental disease, shows the important fact that the interstitial changes are well advanced while the nerve-cells present a normal appearance. He points out the almost constant infection of the intervertebral ganglia in both human and experimental infection by inter-cellular invasion from the periphery to the centre, and comes to the conclusion that the virus acts chiefly upon the interstitial element of the meninges, causing a cellular, chiefly lymphocytic, accumulation, most abundant about the blood-vessels through which various parenchymatous cells become injured and destroyed.

Kling, Pettersson and Wernstedt [64], from their extensive series of experiments, describe two distinct pathological conditions in the monkeys dead of poliomyelitis: the one interstitial, the other parenchymatous:—

(1) The infiltrative type, the pathological picture commonly presented by the spinal cord of monkeys in connexion with experimental poliomyelitis.

(2) The degenerative type, in which cellular infiltration is absent and the striking change is degeneration of the nerve-cells. This degeneration affects not only the nerve-cells, but also the cells of the glia. The authors describe, in fact, two degenerative types: *the one* in which the ganglion cells are encroached upon by a large number of cells which are polymorphonuclear leucocytes and polyblasts, the polyblasts being, according to Wickman, the real neuronophages; *the second*, in which a cell having a large, clear, rounded cell-body eats its

way into the ganglion cell. This the authors designate as "glia-cell neuronophagia."

An important point is the proportion between the cases in which infiltrative and degenerative changes have been observed in experimental animals.

The figures show that animals inoculated from virulent cases give a far greater percentage of infiltrative cases than those inoculated from abortive and convalescent cases:—

	Animals dead	Infiltrative	Degenerative
(1) Typical cases	59 ..	25 (42 per cent.) ..	34 (58 per cent.).
(2) Abortive and virus carriers ..	34 ..	1 (3 ,,) ..	33 (97 ,,).
(3) Convalescents..	23 ..	2 (8 ,,) ..	21 (91 ,,).

The greater virulence and the appearance of the inflammatory infiltration evidently go hand in hand in the monkey. The authors come to the conclusion that the degeneration of the ganglion cells, as well as the cellular and humoral exudation, are to be regarded as the result of a direct injurious influence of the virus. This is a new light in which to regard the action of the virus of poliomyelitis, for in the past the changes in the nerve-elements have been regarded as secondary to the infiltration of the tissues. Further experiments are necessary to confirm or disprove the view expressed by these authors.

The view held by most experimenters is that the changes found in the brain and spinal cord in experimental poliomyelitis do not differ from those found in natural infection. In the spinal cord the lesions are usually more severe and widespread than in the brain. The meninges usually show a more or less diffuse infiltration with round cells. The layers immediately next to the white matter of the cord tend to show more cells than the layers next the dura mater. The greatest accumulation of cells is about the arteries and veins, the sheaths of which are surrounded by cells. The effect of these cells on the lumina of the smaller vessels is considerable. The meningeal cellular invasion is only interstitial, and does not give rise to an exudate upon the surface of the cord or brain such as occurs in acute exudative inflammation.

In concluding this digest of the experimental work, I have endeavoured to put before you the present view of the subject taken by the American and Continental schools. Many questions have been answered, but there are others which are still debatable, and one of the most important is that raised by the clinical and pathological picture produced by Kling, Pettersson and Wernstedt as the result

of these injections. Should their work be established, it will give to poliomyelitis an even wider clinical and pathological aspect than it has acquired during the last decade.

Chapter IV.—"Poliomyelitis" in Animals.

Infection of Animals other than Monkeys and Apes.

Most observers have failed to transmit human poliomyelitis to animals other than monkeys and apes. Flexner and Lewis tried the horse, ox, pig, rat, cat, and rabbit; Levaditi and Landsteiner tried the rabbit, guinea-pig, young dogs, and sheep. Leiner and Wiesner tried young dogs, fowls, pigeons, and rabbits; and Roemer rabbits, guinea-pigs, and mice—all without success [70].

Krause and Meinicke, Lentz and Huntemüller assert that they transmitted poliomyelitis regularly to rabbits. These rabbits succumbed with or without paralytic symptoms, and on histological examination the characteristic changes of poliomyelitis, more or less pronounced, were found. These investigators think that the inoculation into rabbits of cerebrospinal fluid, blood, brain, or spleen obtained from human cases of poliomyelitis leads to the death of these animals, and the inoculation of similar tissues obtained from rabbits that have succumbed into other rabbits will bring about their death. When the injections were made into the blood and peritoneal cavity a greater number of positive results were obtained than when they were made into the brain. The effects could be produced in rabbits, not only with an emulsion of the organs mentioned, but also with Berkefeld filtrates prepared from them. Levaditi once succeeded in transmitting poliomyelitis to a rabbit, and the spinal lesion was even more marked than in a monkey.

Marks [78] has further investigated this question. He used young rabbits; these were injected with an emulsion of the spinal cord from a poliomyelitic monkey; 2·5 c.c. to 3·5 c.c. of the emulsion was injected intravenously and intraperitoneally. The injection had no immediate effect on the rabbit. Some of the animals injected died between the eighth and fifteenth days after injection. When death occurred the symptoms came on suddenly, the final stage being generally ushered in by convulsions and rigidity, and death took place in from ten to thirty minutes after the onset of the symptoms. The post-mortem examination showed hyperæmia of the cortex, but no other striking lesion; and microscopical examination failed to show any further characteristic change. Other rabbits were injected with emulsions from various

organs of the rabbits which died, and some of these rabbits succumbed. The virus was thus passed through a series of six rabbits. From rabbits in the second, fourth and sixth set of the series of rabbits, monkeys were inoculated, and these monkeys all developed typical poliomyelitis.

These results leave no doubt that poliomyelitis can be propagated in certain individual rabbits, and that the virus is not confined to the central nervous system, but occurs in equal amount in other organs. It is probable also that not all strains of the virus can be transmitted to even a small fraction of individual rabbits, and this may account for Roemer and Joseph's failure in a long series. It is thus established that the virus of poliomyelitis can survive and probably be propagated in domestic animals that do not show any of the symptoms of poliomyelitis as it occurs in man.

Roemer [70], who has carried out a large series of experiments on rabbits, does not believe that they are a suitable animal for the investigation of poliomyelitis. He says thirty-one rabbits in four series received large doses of material containing the virus of poliomyelitis by simultaneous intravenous and intraperitoneal injection. The virulence of the material used was proved by the fate of the four control monkeys, which all died of typical poliomyelitis.

Of the thirty-one rabbits, thirty remained well for four months under daily observation, one animal suffered from an atypical form of paralysis, for which no lesion of the nature of poliomyelitis could be made responsible.

The similarity of the virus and of the pathological lesion of poliomyelitis and that of rabies, a disease of which the carrier species is known to be canine, suggest the possibility of some similar animal carrier for poliomyelitis. It is therefore important to investigate the paralyses of animals occurring at the same time as poliomyelitis in man, or of cases in animals presenting similar clinical features or pathological appearances. The simultaneous occurrence of paralysis in fowls and poliomyelitis in man has been noted by Krause, and he refers to other observations of the like nature. He failed to find any pathological lesion in the fowls investigated.

Lust and Rosenberg [74] carried out a series of experiments endeavouring to infect fowls, but they were unable to infect them either naturally or experimentally.

C. S. Shore, veterinary surgeon, refers to a disease appearing in one to two-year-old colts that showed a line of symptoms closely resembling poliomyelitis in children.

Reece, in his report on the epidemic of poliomyelitis in Devonshire, referred to the affection of pigs, to poke-neck in horses, to an affection of fowls, and to the death of a bull and a calf. No pathological examination was made in these cases. He also refers to a large mortality in Sweden of reindeer, poultry, and dogs from a disease stated to be poliomyelitis.

Roemer [79], in 1911, described a disease like poliomyelitis which arose spontaneously in guinea-pigs. The disease was due to an ultramicroscopic organism, which could withstand the action of glycerine and could be transmitted from guinea-pig to guinea-pig by intra-cerebral injections. Monkeys were not, however, susceptible to the disease, and though in its characteristics it closely resembled poliomyelitis, yet it is clear that it is distinct from that disease.

McGowan and Rettie [76] described poliomyelitis in sheep suffering from "loupin ill" and changes in the central nervous system similar to those found in poliomyelitis, but they were not able to transmit the disease by inoculation.

Holmes and myself [71], 1908, have described perivascular lymphocytosis and changes in the central nervous system of a dog which suffered from paralysis, and in 1913 Flexner and Clark [73] described paralysis in a dog simulating poliomyelitis. They were not, however, able to transmit the disease to other dogs by intraspinal inoculation.

Borna disease in horses, again, has a similarity, both clinically and pathologically, to poliomyelitis.

Marchant and Petit [77] describe a case of acute poliomyelitis with symptoms like Landry's disease in a mare. The animal died on the seventh day of illness, and the spinal cord showed foci of inflammation and degeneration of the ganglion cells. No micro-organisms were found. A guinea-pig inoculated with the blood of the mare died on the third day, but the examination showed nothing definite.

McGowan and Dawson [75] compare the lesion of the nervous system in distemper of the dog with those of human poliomyelitis, and come to the conclusion that they are strikingly similar.

The failure to communicate the diseases to monkeys, and in some cases even to animals of their own species, makes it almost certain that the diseases described in animals are distinct from poliomyelitis of man, though bearing some resemblance both clinically and pathologically.

Bruno [72] brought forward evidence of infection from ducks, and the simultaneous appearance of paralysis in a cow and goat.

The relationship of the diseases in animals to those in man is a question which needs most careful investigation.

Chapter V.—Serum Diagnosis.

(1) *Experimental method.*—Levaditi and Landsteiner and Müller have shown that it is possible to test the serum of patients and monkeys for their viricidal properties. For this purpose a 5 per cent. emulsion of the spinal cord containing the active virus is mixed with an equal quantity of the serum to be tested. The mixture must be made at a temperature of 34° C., and stood at room temperature for several hours. It is then injected intra-cerebrally in quantities of 0·6 c.c. to 0·8 c.c. into a normal monkey. A control monkey receives the same quantity of the virus. The control monkey becomes infected, the other monkey remains free. This experiment has been tried with the blood of a patient who has had herpes zoster, but the experiment was inconclusive, as the control monkey was not affected (Müller).

Anderson and Frost found that the blood serum, in six out of nine suspected cases of abortive poliomyelitis, was viricidal against the virus of the poliomyelitis. Landsteiner, Levaditi, Leiner and Wiesner have all shown that the serum is viricidal *in vitro*, but not *in vivo*. The serum injected into animals has no preventive or curative effect. The sera of animals has no viricidal power.

(2) *Fixation of the complement method.*—This point has been investigated by Wollstein, Roemer, Joseph, Levaditi and Landsteiner. All these observers agree that the use of an extract of organs containing the virus as antigen does not permit the discovery of antibodies in the serum or cerebrospinal fluid.

Roemer and Joseph call attention to the fact that this absence of amboceptor is similar to that in rabies, for no amboceptor has been demonstrated in that disease.

Peabody, Draper and Dochez carried out a series of tests with blood sera from—(1) normal persons; (2) from those exposed to infection in the ward or suspected abortive cases; (3) from typical cases, the serum from the patients being mixed with a known dose of the active virus incubated for one to two hours at 37° C., and allowed to stand in ice for twenty-four hours. The injections were then made intra-cerebrally into monkeys. The result was that the sera of the typical cases protected the monkey, but the sera from the normal and abortive cases gave uncertain results. So far no serum test, other than the above, has been devised. Such a test would be of the greatest value, for it would serve to render clear the nature of many cases of certain nervous diseases in children, the cause of which at the present time remain obscure.

Chapter VI.—Clinical Features.

(1) *Forms of Poliomyelitis.*

Recognizing that poliomyelitis is an acute infective disease which may attack any portion of the nervous system, it is at once apparent that the clinical picture may be most varied according to the situation of the lesion. Many observers have collected and tabulated their cases according to the part of the body paralysed, and it has been shown that the legs, and especially the distal muscles, are more commonly affected than any other part. Isolated paralysis of the trunk muscles occurs in about 1 per cent., and isolated paralysis of the cranial nerves in about 2·5 per cent. Wickman's figures show that in 68 per cent. of all cases the legs are affected. Wickman divided the cases into various groups on an anatomical basis, according to the portion of the nervous system involved. The groups are as follows :—

(i) The spinal form.
(ii) The bulbar, pontine and mid-brain form.
(iii) The cerebral form.
(iv) The cerebellar form.
(v) The meningitic form.
(vi) The neuritic form.
(vii) The abortive form.

Peabody, Draper and Dochez [107], in their excellent monograph on the clinical features of poliomyelitis, criticize this classification, saying that it is based neither on pathological anatomy nor on clinical symptomatology, but on a mixture of the two. They prefer the classification suggested by Müller on an anatomical basis—viz. :—

(i) Spinal form.
(ii) Bulbar form.
(iii) Cerebral form.
(iv) Abortive cases.

But even here a clinical type (abortive cases) has to be introduced to complete the classification. No other classification seems to me to be so helpful in the clinical description of the disease as that given by Wickman.

(i) *The Spinal Form.*

This is the common manifestation of the disease, and the type most usually seen is that of a flaccid paralysis of one or more limbs; sometimes all the muscles of both limbs, trunk and neck are completely paralysed. The clinical variations in this form are, however,

considerable and require special notice, for they are not always recognized as manifestations of poliomyelitis.

Ascending and descending type: A type which is not common, and is more frequently seen in adult life than in childhood, is the ascending type (sometimes called Landry type), in which the disease, starting from below, gradually ascends and affects successively the legs,

FIG. 24.—Photo of a boy with paralysis of the intercostal and abdominal muscles and complete collapse of the right lung due to poliomyelitis. The heart is displaced to the right side, as indicated by the shaded area on the chest wall.

FIG. 25.—Lateral view of same case, showing the prominence of the abdomen due to weakness of the abdominal muscles.

the abdomen, the thorax, the arm and neck, so that eventually the respiratory centres are involved and the patient dies from failure of respiration, consciousness often being retained to the end.

This ascending progress of the disease is not always uniform; the disease after affecting the lower limbs, will sometimes cease, and then, after an interval of two to three days or it may be even ten to fourteen,

again start its upward course, possibly again become arrested for a time, and then make further progress until the respiratory centre or the bulb becomes involved. These have been designated the "jump" cases, and experimentally similar manifestations have been noted by Roemer in the monkey [50], and he refers to a similar instance reported by Levaditi and Stanesco.

Sometimes the disease will manifest itself first in the upper segments of the cord, and involve the lower limbs at a later period (descending type).

Thoracic and abdominal type: Sometimes the disease will involve the thoracic and abdominal muscles alone, leaving the limbs unaffected, and in such a case the acute respiratory disturbance suggests the onset of pneumonia. This is intensified when accompanied by complete collapse of one lung. It is difficult to say whether the collapse of the lung occurs at the same time as the paralysis of the intercostal muscles or is due to the blocking of the bronchus by mucus which there is no expiratory effort to expel.

The following case illustrates this condition (fig. 24):—

A. H., aged 4, taken ill in August, 1914, with "pneumonia." Six weeks later he was admitted to the hospital with complete paralysis of the intercostal and upper abdominal muscles, but without any marked affection of the limbs. He had complete collapse of the right lung, and the heart was displaced to the right side. Endeavours were made to expand the right lung without success, and eighteen months later the condition of the lung was unaltered, and the heart in the same position. Respiration is carried on entirely by the diaphragm.

Sutherland [113] has described a similar case in an infant, aged 15 months, with paralysis of the abdominal muscles and collapse of the right lung.

Abdominal muscles: Paralysis of the abdominal muscles frequently accompanies that of the intercostals. The weakness of these muscles gives rise to difficulty in rising from the lying into the sitting position, and to a marked prominence when the patient assumes the erect position (fig. 25). During inspiration it is not unusual to see marked recession of the epigastrium. It is not uncommon to see a partial paralysis of the abdominal muscle, so that when the child coughs or strains there is a protrusion of the abdominal contents into the thinned abdominal parietes, and such a protrusion suggests to the parent that a tumour is growing in the abdomen (fig. 26). Although paralysis of the abdominal wall most frequently occurs in association with thoracic and limb paralysis,

yet it may be absolutely limited to a small portion of the abdominal or oblique muscles, and be the only manifestation of a past poliomyelitis.

Weakness and paralysis of the dorsal muscles of the back prevent the child from assuming the erect position either when sitting or standing. The trunk falls forward and the child is unable to erect it. Such a weakness often gives rise to the saddle-back and to the quadruped walking

FIG. 26.—Photo of girl, showing local bulging of the abdominal wall due to poliomyelitis. (For this photograph I am indebted to Dr. Sutherland.)

adopted by these children as a mode of progress (fig. 27). It is the weakness of these muscles which gives rise to the most marked lateral curvatures.

Transverse lesion: A somewhat rare manifestation of acute poliomyelitis is a transverse lesion of the spinal cord, so that the patient has complete flaccid paralysis of both legs, loss of sphincter control, and loss of sensation to the level of the lesion. This lesion may remain complete, or may clear up, leaving the patient with spastic paraplegia

with increased knee-jerk, ankle clonus, and defective control over the bladder. As illustrative examples the following cases may be quoted :—

F. T., aged 19, was taken ill January, 1914, with fever and pains, and with a rapidly progressive paraplegia which became complete in forty-eight hours, giving rise to an absolutely flaccid paralysis of both legs with loss of sensation to a line 1 in. above the umbilicus. There were retention of urine and an absence of all the deep reflexes. About six weeks later the knee-jerk returned, and eventually both legs became spastic. Sensation also began to return. The examination of the blood and cerebrospinal fluid excluded syphilis. The possi-

FIG. 27.—Boy with extensive poliomyelitis, especially of the extensors of the thighs on the trunk. He was unable to maintain the erect position, and adopted the quadruped method of walking.

bility of an extradural hæmorrhage and tumour was excluded by operation, which revealed a cord presenting almost a normal appearance. The girl, after eighteen months, recovered some power in the legs, but was left in a very spastic condition.

J. D., aged 6, was taken ill on May 2, 1915, with convulsions, fever, pains in the back, and weakness of both legs and arms. The sphincters were affected. He was admitted to hospital August 6, 1915. He had then a very spastic condition of both legs, with considerable adductor spasms and very little power of movement. The knee-jerks were increased, there was ankle clonus on both sides, and the plantars were extensor. No alteration in sensation could be detected. The cerebrospinal fluid was normal, and both blood and cerebrospinal fluid gave a negative Wassermann. The X-rays

showed there was no disease of the vertebræ. On August 14 he developed measles, and during his convalescence therefrom the power in his legs began to improve, the improvement being maintained, so that when he left the hospital on October 25 he could walk fairly well, but was still spastic.

When the lesion is situated in the cervical region, weakness and wasting of the hand and arm muscles, and a spastic condition of the leg, may occur:—

E. D., aged 2, was taken ill in July, 1913, with a rise of temperature, profuse sweating and great pain and screaming attack; his illness was attributed to a circumcision which had recently been performed. After recovering from the acute attack, which lasted about seventeen days, it was noticed that he could not move his hands, and was very weak in the legs and back: it was also noticed that his knee-jerks were brisk and ankle clonus was present. When seen in October, 1913, there were marked weakness and wasting of the small muscles of both hands, drooping of the eyelid (probably due to sympathetic affection), a spastic condition of both legs with increased knee-jerks, ankle clonus and extensor responses; no sensory defect. The X-rays showed no disease of the cervical vertebræ. The boy slowly improved, but two and half years later still had marked weakness of the small muscles of the hand and a spastic condition of the lower limbs.

It is admittedly difficult in the cases like those above quoted to give positive proof that the lesions were due to the virus of poliomyelitis, for such cases rarely die, so that pathological and experimental evidence is wanting. It has not been possible to carry out the serum test. But by excluding the common causes of transverse lesion one is justified in suggesting that poliomyelitis may be the causal factor.

B. Sachs [110] records a case of acute poliomyelitis in a girl, aged 18, with sudden onset of complete flaccid paralysis and loss of sensation to the xiphoid with complete recovery in two months. The cerebrospinal fluid showed a high lymphocytic count.

Netter and Levaditi [103] report four cases presenting symptoms of transverse myelitis which they attribute to the virus of poliomyelitis. They were able to show that the blood of a patient who had recovered possessed the properties for neutralizing the virus of poliomyelitis.

Strümpell [112] records a case in a man, aged 19, of sudden onset of paralysis of the arms with considerable loss of sensation in the trunk and leg below the seat of the lesion. This lesion he attributes to poliomyelitis. Similar observations have been made by others.

Abnormal attitudes assumed in incomplete paralysis: When all the muscles of a limb are involved a complete flaccid palsy results, and no abnormal attitude is assumed or deformity produced; but in many

instances certain groups only are involved, and the contraction of the unbalanced antagonistic muscles gives rise to unusual position and deformities. The two following cases illustrate this point. They must, however, be considered rather unusual manifestations of the disease. The first is that of a child in whom the extensors of the right thigh were completely paralysed, whilst the flexors were unaffected, the result being that the leg was held erect in the air as the child lay in bed (fig. 28).

In the less extreme examples of this form the leg is held out in front, and gives rise to a difficulty in walking quite out of proportion

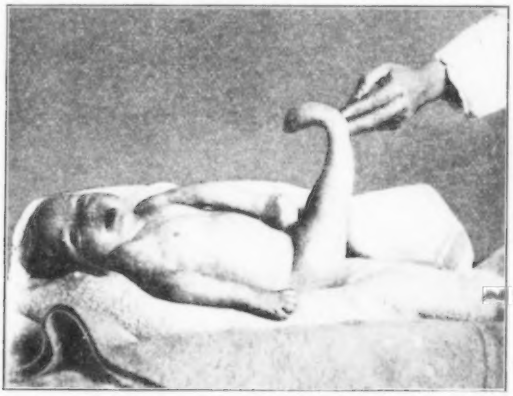


FIG. 28.—Infant with poliomyelitis of both legs and arms, the right leg is held erect in the air owing to the paralysis of the extensors of the thigh and the unbalanced contraction of the flexors. The leg is being steadied by the hand of an observer for photographic purposes.

to the weakness of the limb, and the attempt to bring it into line with the trunk only produces a lordosis, or the trunk is bent forward with a loss of balance. When this deformity is bilateral the lordosis becomes marked, and the child can only assume the erect position by an extreme lordosis of the spine (fig. 29).

The reverse of the above condition is seen in the case of a child in whom the flexors of the thigh are paralysed, whilst the extensors are unparalysed and in active contraction. Such a condition gives rise to a rigid child, the legs cannot be flexed and the child can be supported by the head and heels, and held out in a rigid position such as shown in fig. 30. The case is as follows :—

FIG. 29.—Girl with extensive poliomyelitis and bilateral contraction of the flexors of the hip-joints.
In the attempt to assume the erect position a lordosis of the spine is produced.

FIG. 30.—Child with extensive poliomyelitis, showing rigid extension of the hips, due to the unbalanced action of the gluteal muscles. This rigidity was such that the child could be supported by one hand placed under the head, and the other under the heels.

Poliomyelitis with rigid extension of the legs at the hips: H. G., the fifth child of a family of five, was taken acutely ill with poliomyelitis in September, 1912, the limbs, trunk, face and eyes being affected at the onset. He was acutely ill for fourteen days, then gradually recovered the power in his right arm, but had severe pain and tenderness in trunk and lower limbs. When seen in March, 1913, both legs were rigid at the hips and everted, and attempts at movement caused acute pain. Below the knee the muscles were flaccid and the feet in a position of equinus. The shoulder muscles of the left arm were completely paralysed, and there was likewise considerable intercostal and abdominal paralysis. The child was quite rigid in the extended position, and if lifted off the bed by one hand placed under the head and another under the heels, he maintained this extended position (fig. 30). This rigid extension of the hips appeared to be due to the unbalanced action of the gluteal muscles, the psoas and the iliacus muscles being completely paralysed. Any attempt at flexion of the hip gave rise to pain, but if once flexed, the hip-joint could be moved in any direction quite easily. X-ray examination made it certain that there was no hip disease. All the deep reflexes were abolished in the lower limbs. The pain on movement in this case persisted for over fourteen months. In this case the child was up in plaster of Paris in a position of flexion, so as to overcome the extension and allow the flexors to recover. Although the child was kept for months in this position, yet he always, in a few days after the plaster was removed, reverted to the rigid extended position. It is interesting to note that when first taken out of plaster the legs remained in the flexed condition for a few hours. Massage, movements, hot baths, had no effect, either in overcoming the rigidity or of removing the pain on movement.

Paralysis of neck muscles: In some cases the neck muscles may alone be affected, so that the head flops about in all directions. In one case the affection was almost limited to the neck muscles, the shoulder muscles being but slightly affected, whilst the muscles supplied by the bulb escaped entirely; the diaphragm, too, was unaffected (fig. 31):—

William F., aged 11, was taken acutely ill in March, 1915. He had severe headache, vomiting and constitutional symptoms; one week after onset a measles-like rash appeared which lasted two days. He had, when seen ten days after the onset, some weakness of shoulder muscles and complete flaccid paralysis of the neck muscles, being quite unable to hold the head up. He at no time had any bulbar symptoms. He could move the arm well and had full power in the thoracic, abdominal, and leg muscles. He was quite unable to sit up or walk, owing to the weakness of his neck muscles. The cerebrospinal fluid was clear, contained 0·15 per cent. albumin, no cells, and gave a negative Wassermann reaction. The neck was splinted (*see* fig. 43), and the boy gradually recovered power, but considerable weakness of sterno-

mastoid and trapezius remained. He could walk quite well as long as his head was supported by the splint.

Unilateral paralysis of the diaphragm: The diaphragm may be affected at the same time as the intercostal muscles, and sometimes one

FIG. 31.—Boy with complete flaccid paralysis of neck muscles, those supplied by the bulb escaped entirely (compare fig. 43), and the limb muscles almost entirely.

FIG. 32.—Unilateral paralysis of the right side of the diaphragm (from an X-ray kindly lent by Dr. Voelcker).

side of the diaphragm is involved whilst the other moves well. This is best seen on an X-ray screen, when the movements can be watched (fig. 32).

Sympathetic paralysis: Paralysis of the sympathetic fibres has been noted in cases of poliomyelitis in the region of the first dorsal and lower cervical segments of the cords, but no observations have been made on the occurrence of subnormal temperature such as is known to occur and has recently been noted by Gordon Holmes in the Goulstonian Lectures in injury to the lower cervical region of the spinal cord.

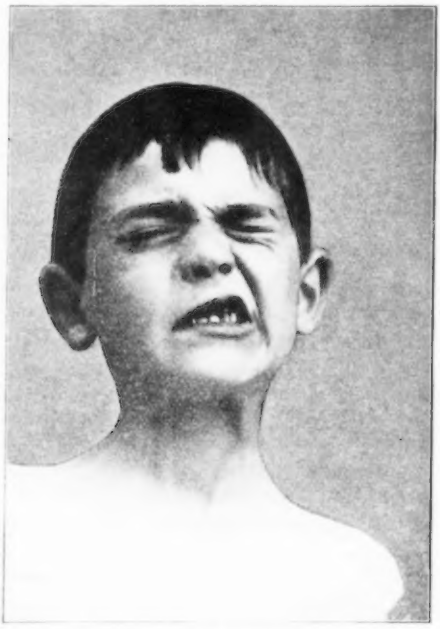


FIG. 33.—Paralysis of the right side of the face, associated with flaccid paralysis of the muscles of the right shoulder.

(ii) *The Bulbar, Pontine and Mid-brain Form.*

Bremer [85], in an analysis of 400 cases of poliomyelitis from the records of the Children's Hospital, found that forty-eight—i.e., 12 per cent.—showed some evidence of an encephalitis, facial paralysis being the commonest manifestation, whilst ataxia, nystagmus and tremor formed the next most numerous group. The clinical manifestations exhibited by lesions in this region are most varied. Any extensive lesion in the bulb is almost always rapidly fatal, and a typical instance of such with a good pathological examination is recorded by Feiling [90].

The acute symptoms may be severe, yet they will often clear up, leaving a paralysis limited to one or more cranial nerves.

Lesions in this region may affect any one or more of the cranial nerves; that which is most commonly attacked is the seventh, giving rise to a facial paralysis of the lower motor neuron type (fig. 33). When such a paralysis is associated with a poliomyelitic lesion in the cord, causing a limb paralysis, or when another member of the family is affected with the ordinary type of poliomyelitis at the same time, it is not difficult to recognize the nature of the affection; but when the facial paralysis occurs as the solitary manifestation, considerable difficulty arises in regard to the diagnosis. It has been noted that the number of cases of facial paralysis among children tends to increase with the prevalence of poliomyelitis.

Of the other cranial nerve nuclei, those supplying the tongue, the palate, the masseter and temporal muscles may be affected, either unilaterally or bilaterally. The oculo-motor nuclei may be affected, giving rise to a complete or partial ophthalmoplegia. Blindness is sometimes associated with the paralysis. Return of vision and complete restoration of power in the muscles may take place, or the ocular palsy may clear up, leaving the child completely blind. I have recorded such an association in a child:—

M. S., aged 5½, taken ill acutely with headache, followed by loss of sight and complete ophthalmoplegia externa: the opthalmoplegia cleared up almost entirely in a month, leaving the child, however, completely blind. There was slight swelling of the disk, but not a marked optic neuritis.

That poliomyelitis may, in some cases, account for the sudden loss of vision and of hearing is possible, but pathological confirmation has not been obtained.

Associated myelitis and optic neuritis: E. Clowes [86] records a case of acute myelitis with optic neuritis in which the sudden onset, the character and progressive nature of the symptoms, with death on the fourteenth day of illness, strongly suggest the possibility of poliomyelitis as the causative factor. Unfortunately no pathological examination was obtained.

Dr. Frederick Taylor [114] alludes to the association of optic neuritis with spinal lesion, of which there are a number of recorded instances. Many of these cannot be attributed to poliomyelitis. It is, however, the acute and sudden onset of both spinal and ocular symptoms which is the feature which so strongly suggests the poliomyelitic infection.

Hertz, Johnson and Depree [96] record the case of a boy, aged 12½,

who had acute onset of paralysis with optic neuritis and ocular palsy. The cerebrospinal fluid showed lymphocytosis and polymorphonuclear cells in almost equal numbers. The boy recovered to a very considerable extent. The authors regard this as a case of polio-encephalo-myelitis.

Mid-brain lesions: The symptom most characteristic of lesions in mid-brain is that of a rhythmic tremor of the limbs associated with an ocular and sometimes other cranial nerve paralyses. Holmes has described the tremor of mid-brain lesion as a slow regular tremor, increased by involuntary movement and by excitement. It may be universal and affect the whole body, but in most cases is limited to the limbs and is seen in its most typical form in the arms. There is an increase of tone and some disability in using the limb, but there is no true spasticity, and the limb is in a condition of "plastic tone." As illustrative of this condition the following case, recorded by Leonard Parsons [106], may be quoted:—

A girl, aged 2, was at play and apparently quite well on the evening of July 15. She was put to bed and noticed to be feverish. At 10 p.m. she had a fit, became sleepy and unconscious. At 10 a.m. and 12 noon she had a recurrence of the fits. On recovering consciousness it was noticed that she was trembling all over; the tremor affected the tongue, arms, legs and trunk, and was exactly like shivering. For three weeks she remained in bed, during which time the tremor persisted; she was apparently conscious, took her milk, but her eyes were fixed and staring and she did not appear to see anything, nor did she speak. When admitted to hospital on August 2, there was slight retraction of the head, her expression was staring and she was apparently quite blind. There was present a slow, rhythmic tremor of the arms with marked rigidity of the limbs, but no evidence of paresis. The knee-jerk and abdominal reflex were present, and the plantar responses were flexor. Both pupils reacted to light, and the fundi showed no change. There was broncho-pneumonia. The cerebrospinal fluid was examined and no lymphocytosis or organisms were found. On August 24 the child spoke for the first time, and it was noticed that her vision had returned. On September 4 the tremor was no longer present whilst the child was at rest, but was brought out by voluntary movement. She left the hospital on September 12, but she still had some tremor on voluntary movement. She was seen again in February, 1910, when she appeared well and talked freely.

Other cases occur in which ocular palsy and nystagmus are present, and others again in which there is evidence of involvement of the fifth, sixth and seventh cranial nerves, the variation in symptoms depending on the situation and extent of the lesion.

It may be well to mention here the movements which Netter and Ribadeau-Dumas [104] describe as chorea occurring before and during

the onset of acute poliomyelitis, and these are probably of the same nature as those described by Colliver [87] under the name "A pre-paralytic symptom in acute poliomyelitis" as a tremor and convulsion of certain groups of muscles.

(iii) *Cerebral Form.*

The most characteristic feature of this type is hemiplegia. The onset of the illness is sudden, associated with convulsions, which may be unilateral or bilateral, and loss of consciousness, and the child, on recovery, is found to be hemiplegic. Poliomyelitis is probably not a frequent cause of infantile hemiplegia. Of 100 cases of infantile hemiplegia collected by myself, only ten could on clinical grounds alone be ascribed to polio-encephalitis, the criteria for such being that the child was perfectly healthy before the onset, the onset was sudden, that it occurred during the summer months, and the symptoms were retrogressive after the attack was over, and that there was no cardiac or other condition likely to give rise to a hemiplegia.

Should the hemiplegia be associated with a poliomyelitis of the limbs, it may with reasonable probability be assumed that the lesions are due to the same causal organisms, and a striking instance of such an association has been published by Rossi [109], the diagnosis being verified by a pathological examination, to which allusion has already been made in the section dealing with pathology.

An American writer, Manning [99], tries to prove that the attack of hemiplegia from which Pasteur suffered at the age of 46 was due to a poliomyelitis—the infection being derived from the silkworm, Pasteur being engaged on that work at the time.

Athetosis of left arm and left side of face, flaccid paralysis of left leg, and some flaccid paralysis of right leg: The association of a hemiplegia with athetosis with a poliomyelitis is one of the rarest manifestations of the disease, and the following instance may be given:—

A. A., aged 7, was the seventh of eight children. She was a healthy baby till the age of 10 months, when she had an acute illness with convulsions. From this she recovered, but it left her with paralysis of the left side. She subsequently learnt to talk, was intelligent, and went to a school for physically deficient children. She never learnt to walk. When first seen she was a pale child, with marked athetosis of the left arm and involuntary movements of the left side of the face. She was unable to stand, and if an attempt were made to place her on her legs, she supported her weight on the right leg with the knee flexed, the left leg being too weak to support any weight. The left hand exhibited spontaneous movements of an athetoid character (fig. 34),

which were increased on attempting to walk or on any emotional stimulus. The child had little voluntary power of movement in the left hand; there was, however, no rigidity, and the hand, though at times strongly contracted, yet when moved passively was quite flaccid. The left leg showed the typical flaccid palsy of poliomyelitis with wasting of muscles, loss of deep reflexes, and loss of electrical reaction of all muscles below the knee, and to a lesser degree above the knee.

FIG. 34.—Athetosis of the left arm and left side of the face, associated with a flaccid paralysis of the left leg, and partial paralysis of the right leg.

This case illustrates the association of an athetosis with a poliomyelitis. There is no reason to doubt that the paralysis of the legs is due to a spinal lesion, and the athetosis of arm and face to a cerebral lesion. It may be questioned whether there is sufficient evidence to prove that the condition is the result of the virus of poliomyelitis, but, so far as the legs are concerned, they may be considered typical of the condition. The arm paralysis occurred at the same time, and there

seems no reason for hypothesizing another toxic condition for the production of the focal lesion in the brain. The contraction which was present in the legs has been corrected, and with support the girl walks fairly well. The athetosis of the left arm persists.

Mental defect: Cases in which marked mental defect persists after an acute cerebral attack in children are not uncommon, but the difficulty of proving that such cases are due to poliomyelitic virus is considerable. Such cases may or may not be accompanied by an alteration in the cerebrospinal fluid. When accompanied by a lympho-

FIG. 35.—Child with acute cerebellar ataxia attempting to walk. The nurse is preventing the child from falling backwards, a tendency which such cases commonly exhibit. Note the wide base and the spread arms.

cytosis the cases come within the meningeal group and are dealt with under that head, but those cases in which the fluid is perfectly normal correspond closely to those in which the poliomyelitic virus affects other portions of the brain and spinal cord, no change being found in the cerebrospinal fluid.

The cases of this type have always been isolated, and I have never seen this form in one member of a family in which others have typical poliomyelitis. Pathological proof of the nature of the affection has not been obtained.

(iv) *The Cerebellar or Ataxic Form.*

This type is characterized by the acute onset of ataxia, sometimes associated with ocular and other cranial nerve paralyses and alteration of articulation. Nystagmus is often absent. As with other forms of poliomyelitis, the onset may be attended by malaise and vomiting, but in other cases the onset is quite sudden, and the child having gone to bed perfectly well, is found in the morning to be wildly ataxic, but otherwise not ill. In some cases the ataxia clears up rapidly, so that after ten to fourteen days the child is quite well. In other cases it takes many months and sometimes years to clear up.

An interesting instance of slow and gradual recovery in a boy who, after an acute illness, was ataxic for some three years has been recorded by Dr. Frederick Taylor [115]. When seen some twenty-five years later he was in every respect a normal individual, and had been so during boyhood and manhood, having played the usual games necessitating good co-ordination.

The following is an instance of one child in the family being affected with the ordinary type of poliomyelitis and another with ataxia:—

Poliomyelitis and ataxia: probably due to involvement of the cerebellum: R. S., aged $5\frac{1}{2}$, and M. S., aged $1\frac{1}{2}$, are brother and sister, and they were both taken acutely ill within a week of one another on August 16, 1909. The elder child had left facial paralysis and ataxia of the right arm and leg, whilst his sister had paralysis of the left side of the face and flaccid palsy of the neck muscles. In the elder child the ataxia cleared up in about fourteen days after the onset of the acute illness. The paralysis of the face cleared up somewhat later. In the case of his younger sister the weakness of the face persisted for many months, as did also the weakness of the muscles of the neck, some permanent paresis of the neck muscles remaining. In these two cases there is no doubt that the paralysis was due to acute poliomyelitis, and in the case of the older child it seems probable that there was a focus of the disease in the cerebellum.

Numerous other instances of acute cerebellar ataxia might be quoted, some of which have cleared up rapidly, and others have persisted for months and years.

In those cases in which ataxia of sudden onset is the only symptom it may well be doubted if they are caused by poliomyelitic virus, but the same cannot be said of those cases in which the ataxia is seen in conjunction with other more usual manifestations of the disease, or in such cases as those in which one member of the family has definite poliomyelitis and another is affected with ataxia.

That the lesion is in the cerebellum also may be questioned, for there is but little pathological evidence on these cases, but as the clinical signs closely correspond with those seen in definite lesion of the cerebellum, there is little doubt that the lesion lies somewhere in the cerebellar path.

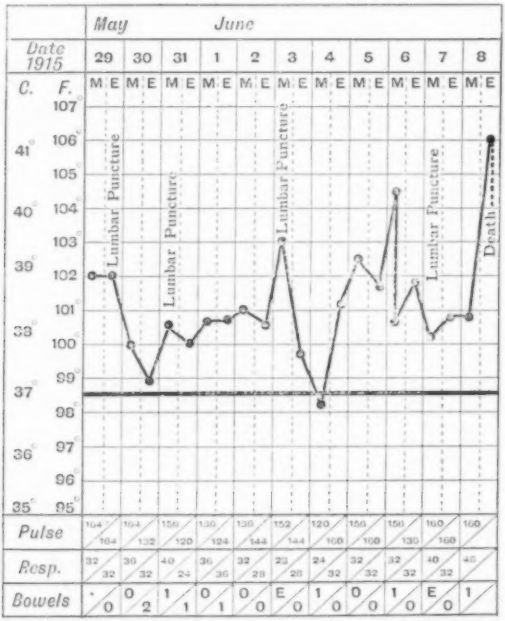
(v) *Meningitic Form.*

Possibly one of the most interesting groups of poliomyelitis, and one which frequently leads to an error in diagnosis, is the meningitic form of the disease. The onset may be sudden, attended by convulsions and coma. This may rapidly pass off, or persist and deepen. Temperature is raised and may remain high for days. The neck is stiff, and the legs rigid in a flexed or extended position, and Kernig's sign may be present. The pulse is slow or rapid, according to the stage of the disease. All the symptoms of a meningitis may be present, and on lumbar puncture the cerebrospinal fluid escapes under pressure, is clear, and on cytological examination may be found to contain an increased number of lymphocytes with a normal, or sometimes a diminished sugar reaction and increased amount of albumin.

The cases thus present the clinical picture and cytological condition of the cerebrospinal fluid which is of frequent occurrence in tuberculous meningitis. If tubercle bacilli are found in the cerebrospinal fluid the diagnosis is clear, but if not found the case falls into the group of lymphocytic meningitis from which recovery is possible. The causes of a lymphocytic meningitis are numerous, and from the examination of the cerebrospinal fluid alone it is not possible to be certain that one is not dealing with a serous meningitis associated with a sinus thrombosis, middle-ear disease, cerebral abscess; with that following mumps or measles; with that due to syphilis or an old and past infective meningitis or to poliomyelitis. As illustrative instances of the meningeal form the following cases may be quoted :—

G. Y., aged 3, was taken ill on June 30, 1913, with sore throat. He was feverish for two or three days. On July 3 he had pains in the back, he cried when moved, and the back was stiff. He was admitted to hospital on July 8 and then had marked retraction of the head and opisthotonos. Any movement of the neck in a forward direction gave rise to pain, but he would allow rotation. There was no rigidity of arms or legs, and the power was good, except in the left leg, which was completely flaccid. On lumbar puncture the cerebrospinal fluid was under pressure, was clear, contained 0·1 per cent. of albumin, no clot, and no cells. The rigidity of the back gradually passed off, but he was left with a flaccid paralysis of the left leg, which recovered to a very great extent after a year's treatment.

R. W. M., aged 5, a patient under the care of my colleague, Dr. Colman. Six weeks previously had measles, from which he rapidly recovered. He came home from school with headache May 26; in the evening he vomited. On the following day he had headache and frequent vomiting. He was feverish. On the morning of May 29 he became convulsed, was delirious, and no longer recognized his mother. He was admitted to hospital, and temperature was 102° F., pulse 164, respiration 32; he was semi-conscious, the neck was rigid, limbs rigid and extended. The cerebrospinal fluid was clear, under increased



Temperature chart of a case of poliomyelitis which presented symptoms similar to those occurring in tuberculous meningitis. Case proved to be poliomyelitis by microscopic examination.

pressure, contained no increase of cells and no albumin, and gave an immediate reduction with Fehling's solution. The condition progressed, the temperature remained high, the cerebrospinal fluid, examined on four occasions, first revealed no cells, then a few, and on the last occasion (June 7) were numerous and were lymphocytic in character; the fluid still reduced Fehling's solution. The boy died on June 8, fourteen days after the onset of the disease. At the autopsy there was no macroscopic meningitis, but on section through the crus and mid-brain marked engorgement of the vessels was found, and on microscopical examination a most extensive perivascular lymphocytosis was present. The spinal cord showed no change.

A third case is that of a boy, aged 4, who six weeks previously had had his tonsils and adenoids removed. He was taken ill on November 16; on November 17 he was feverish, passed into a comatosed condition, was admitted to hospital on the 18th and died on the following day. He was regarded as a case of meningitis, but the lumbar puncture revealed a blood-stained fluid from which it was not possible to make any deduction. *Post-mortem* examination showed extravasation of blood in the region of the cauda equina, possibly due to the lumbar puncture, otherwise the cord appeared to the naked eye normal. On microscopical examination, however, typical poliomyelitic changes were present, most marked in the medulla and in the wall of the fourth ventricle (fig. 18). No change was found in the cerebral hemispheres.

The fourth case is that of a child who presented symptoms of a lymphocytic meningitis with rapid recovery. The details are as follows:—

Betty B., aged 3, the only child of the mother's second family, was taken ill with an attack of vomiting on Friday, September 24, 1915. She was said to have "lost herself" and to have been queer ever since. Her spine seemed to give way and her head was bent to one side. She cried when disturbed and complained of pain at the back of the neck. She was brought to the Hospital for Sick Children, Great Ormond Street, on September 29, 1915, and admitted with the diagnosis of "posterior basic meningitis." On admission, she was a well-nourished child; did not look seriously ill. The temperature was 97° F., pulse 96, and respiration 24 per minute. She sat up in bed of her own accord but held the head towards the right side. On physical examination of the chest and abdomen nothing abnormal could be detected. All movements of the limbs were perfect, but there was slight stiffness of the head and neck and she resented movement. All the deep and superficial reflexes were normal; the optic discs were normal. Kernig's sign was not present. Lumbar puncture was performed and a slightly turbid fluid, just blood-stained, was obtained, which on examination was shown to contain 0·5 per cent of albumin, failed to reduce Fehling's solution, and contained a large number of cells, nearly all of which were mononuclear; no organisms were seen, and the culture on the placenta agar remained sterile; no tubercle bacilli were found. From the examination of the cerebrospinal fluid the most probable diagnosis would seem to be tuberculous meningitis. On October 1 a second lumbar puncture was performed. The fluid again was slightly turbid, formed no clot, gave no immediate reduction of Fehling's solution, contained 0·5 per cent. albumin and a large number of mononuclear cells. No tubercle bacilli were found. On October 8 the child could move the head and neck well and seemed almost normal. Lumbar puncture was performed and the cerebrospinal fluid appeared clear, had no clot, contained 0·125 per cent. albumin, gave *no* immediate reduction of Fehling, and contained a fair number of mononuclear cells (lymphocytes). Cultures on agar were sterile and on placental agar

anaerobically after three days gave two colonies of *Staphylococcus albus* (contamination). On October 12 the cerebrospinal fluid was again examined; it was clear, the albumin was 0·025 per cent., there was slight immediate reduction of Fehling and was still a *very* slight excess of lymphocytosis; cultures were sterile. A Wassermann reaction of the blood and cerebrospinal fluid was negative. The child left the hospital quite well on October 20.

The last recorded case is clearly one of lymphocytic meningitis (serous meningitis), but the cause is obscure. Tubercle as a cause of the meningitis can in this case be fairly excluded. The case does not correspond to the type of lymphocytic meningitis recorded by Gordon, in that the child rapidly recovered; there was no evidence that this child had recently had mumps or measles. Poliomyelitis as a cause seems probable, but it could not be proved.

The four cases just recorded serve as illustrative examples of the meningeal form of poliomyelitis. Clinically they differ from one another considerably. The first presented clinical symptoms which would suggest the acute onset of meningitis. The second presented features similar to those seen in tuberculous meningitis and died after fourteen days. The third was a fulminating case, passing rapidly into coma, and dying in three days. The fourth was a case in which the symptoms were slight, but the change in the cerebrospinal fluid was marked. The first rapidly recovered, leaving a paralysed leg. The second and third were proved by pathological examination to be cases of poliomyelitis, and the fourth case recovered completely from the lymphocytic meningitis, which was probably due to the poliomyelitic virus, but not proven to be so.

R. Morichau-Beauchant, Guyonnett and Corbin [102] give an account of two sisters, aged 4 and 5 respectively, the elder of whom had a definite attack of poliomyelitis accompanied by paralysis of right leg and left arm, and a week later the younger sister had meningitis from which she recovered completely.

(vi) *The "Neuritic" Form.*

Most observers are willing to accept the above forms of the disease, even when direct pathological evidence is not forthcoming; but few are willing to accept the "neuritic," for the clinical picture is so entirely different from that which takes place in other forms of poliomyelitis, and pathological evidence is almost non-existent.

If the presence and persistence of pain are taken as evidence of the "neuritis," then it may be asserted that there is no justification for the

title, since both these symptoms are well-recognized clinical manifestations of the common poliomyelitic lesions of the spinal cord.

If, however, there is an acute illness followed by weakness and wasting of the peripheral muscles, which affects all the extremities more or less symmetrically, and at the same time there is loss of sensation in the peripheral portion of the limbs with tenderness of the muscles, then it will be justifiable to regard the case as one of "toxic neuritis." If such a case occurred with a sudden onset or in association with a typical case of poliomyelitis in other members of the same family or household, it would be justifiable to assume that the same poison was the causative factor.

Some support in favour of the view that the virus of poliomyelitis can sometimes act as a direct toxin to the ganglion cells is to be obtained from the experimental poliomyelitis in monkeys made by Kling, Pettersson and Wernstedt, to which reference has already been made (p. 156). That the virus of poliomyelitis may sometimes act as a direct poison to lower motor neurons seems not improbable. It has been pointed out that mumps, like poliomyelitis, may give rise to a lymphocytic meningitis. Toxic polyneuritis may follow mumps, and the cases recorded by Joffroy [98], Revillion and Gallavardin [92] are instances of such.

Joffroy's case was that of a little girl, aged $6\frac{1}{2}$, who on the eighth day of mumps had pain in the limbs and violent itching. On the twentieth day a flaccid paralysis of the four limbs set in, with complete abolition of reflexes. Cutaneous sensation was blunted. The child eventually made a complete recovery.

In the cases of toxic neuritis of unknown origin in children which have come under my observation, it has not been possible to obtain experimental evidence that the child had been, or was, suffering from the poison of poliomyelitis, and in those cases which died the pathological picture is that of a primary degeneration of the lower motor neurons, not of an infiltrative poliomyelitis. Lead, arsenic, alcohol, diphtheria and sepsis are the common cause of a toxic neuritis; mumps and syphilis rarely give rise to the typical clinical picture of a toxic neuritis, and it is only these last two which can be said to act in the two different methods: (1) by producing a lymphocytic meningitis; and (2) as a direct poison to the nerve-cell.

It has not been shown either in man or in monkeys that mumps can give rise to a perivascular lymphocytosis of the spinal cord, although it gives rise to a marked perivascular lymphocytosis in the parotid gland.

It would appear that the virus of mumps, although similar to that of poliomyelitis in many ways, has no tendency to affect the nervous system, though rarely it may do so (Gordon) [95].

Wickman discusses the question of poliomyelitic neuritis at some length, and gives illustrative cases. As evidence that poliomyelitis may produce toxic polyneuritis the following cases may be quoted.

James F., aged 16, a milk-boy. In July, 1910, he had some pain in both legs. On July 30 he was taken acutely ill, vomiting for three days; had pain in the abdomen and legs. On August 3 he could not stand, and after that the legs gradually got weaker, and after a few weeks he was absolutely unable to move them, and he could not feel below the knees. He had been in bed for two and a half months, and after the seventh week in bed his legs began to get better; the arms were never much affected. He came under my care in November, 1910. He had then weakness of the arms, feeble grasp, generalized wasting; the trunk-muscles were good; the legs were wasted below the knee; he had double foot-drop, absent knee-jerks, absent ankle-jerks. Electrical changes of the character of reaction of degeneration were present in the muscles of arms and legs. The loss of sensation had cleared up when seen in November, 1910. There was no evidence of lead or arsenic. He recovered under treatment, and was discharged well in January, 1911.

The case was obviously one of toxic neuritis. The only question was, What was the nature of the toxin? The sudden onset of symptoms during the month of August suggested the virus of poliomyelitis as the cause; the proof could only be furnished by experiments on animals, and that was not done.

A. L., aged 30, was, early in May, 1913, taken suddenly ill with weakness of the legs so that she could hardly walk when she attempted to get out of bed in the morning. She had been perfectly well the night before; she had a squint at this time. Since the onset the legs had been steadily getting worse, and when seen some four weeks after the onset there were bilateral foot-drop, tenderness of the muscles, loss of all forms of sensation below the knee, and weakness and some slight anæsthesia of the hands. The knee-jerks were absent. Complete recovery took place. The clinical picture was clearly one of toxic neuritis. What the toxin was must remain doubtful, but the sudden onset suggests the possibility of the virus of poliomyelitis as the cause.

I do not think it can at the present time be asserted that toxic polyneuritis has been *proved* to be a manifestation of the virus of poliomyelitis; but considering the fact that the virus of syphilis and mumps may give rise to the clinical picture of toxic polyneuritis, and the experimental evidence that the poliomyelitic virus does in some cases act as a direct poison to the neurons—there is reasonable ground

for suggesting that polyneuritis may sometimes be a manifestation of the virus of poliomyelitis.

The question would be solved if there was a simple specific blood reaction for poliomyelitis, and it were possible to carry out the test over a sufficient number of cases; but such has yet to be determined.

(vii) *Abortive Form.*

In this country and in London, where it may be said that poliomyelitis has never become epidemic, it is not possible to describe an abortive type of the disease. Reece, in the Stoke Rivers epidemic in Devon, described a large number of cases of indefinite illness which might possibly be cases of this nature; but the proportion of these to actual cases of paralysis was so large that it is difficult to accept them as such.

Wickman, in the Swedish epidemic of 1905, and Kling, Pettersson and Wernstedt in that of 1911, were able to recognize a considerable proportion of abortive cases as occurring in the members of households in which definite cases of poliomyelitis were present.

The picture of the abortive type as given by Wickman corresponds in general with that of the initial stages of typical poliomyelitis. The attack as a rule is acute, and accompanied by fever, headache and malaise. In some cases these symptoms are associated with others, such as rigidity in the neck, pain in the neck, back, loins and limbs, and paræsthesia, which point to infection of the nervous system.

These symptoms are not followed by paralysis. The patient usually recovers within a few days, and no trace of the disease remains, except prostration, which may be prolonged. The abortive case thus presents only symptoms of general infection, and no real localizing signs. In the abortive cases not infrequently symptoms attributable to meningeal irritation arise. More or less opisthotonus may occur. Tenderness of the extremities is common. Nausea, vomiting and diarrhœa and other gastro-intestinal symptoms have frequently been observed in association with the abortive types.

Wickman distinguishes the following varieties of the abortive type:—

(1) Cases running the course of a general infection.

(2) Cases in which signs of meningeal irritation are especially prominent.

(3) Cases accompanied by distinct tenderness.

(4) Cases with gastro-intestinal disturbances.

(2) *Relapsing Cases of Poliomyelitis.*

Reference has been made to the so-called "jump" cases of poliomyelitis in which the disease is not steadily progressive, but remains stationary for a day or two, and then rapidly advances.

Relapsing cases differ somewhat from the above in that the patient improves in the interval, and it is thought that he is going to recover. Then fresh symptoms develop, which may again clear up, and then a further relapse may occur. A very good instance of such a relapsing case with a pathological verification is recorded by Reginald Miller [100]:—

A little boy, aged 3½, was taken ill on September 14, became drowsy, unable to move. The lower limbs were completely paralysed and the neck muscles partially so; the arms and respiratory muscles were unaffected. The boy progressed favourably till September 25th, when he became dyspnœic and cyanosed, and it was found that the intercostals and rectus abdominis were paralysed. He improved, but on October 1 a second relapse occurred, and the muscles of the left shoulder became powerless. From this date there were no fresh signs until October 17, when there developed suddenly a very marked nystagmus, lasting three to four days, gradually becoming less and less marked until the twelfth day, when it was no longer observable. During his further stay in hospital he steadily improved, and was discharged on January 3. A week later he developed broncho-pneumonia and died on January 12. The pathological examination was made by Dr. Gordon Holmes, and the specimens showed the typical appearance of a poliomyelitis, not only in the cord, but also in the medulla, pons, cerebellum, and mid-brain.

(3) *The Occurrence of Second Attacks of Poliomyelitis.*

It is well recognized that progressive muscular atrophy may occur in a patient who during early life has been the subject of poliomyelitis. A series of twenty-eight such cases is recorded by Potts [108] and they are not very rare. In eighteen the atrophy occurred in the limb previously affected; in the remainder in some other part.

The occurrence of a second attack of poliomyelitis is very rare; no such case has come under my observation. Eshner [88] records the case of a girl who had an attack of poliomyelitis when 25 months old, the right lower extremity being affected, and a second attack, attributed to a fall, in the hands eleven years later. Oulmont and Bandouin [105] record another case in a man, aged 60, who within a year had a second attack and died. The *post-mortem* showed changes in the anterior horn and in the muscles. A third case is recorded by Sanz [111], in a girl who had the first attack when 1 year old, affecting left leg and foot,

and the second attack at the age of 15, when the right arm and right leg were affected. Not one of these cases appears to me to be very convincing or to bear critical investigation.

(4) *Intra-uterine Poliomyelitis.*

The occurrence of poliomyelitis in the fœtus during intra-uterine life is very difficult to prove. Not a few cases come under observation in which the paralysis is stated to have been observed immediately after birth; and when the child has come under observation the clinical features closely resemble the late effects of a poliomyelitis.

Flaccid paralysis of one arm due to birth injury is far from uncommon in infants, and in most cases is probably due to injury of the roots of the brachial plexus. It has been shown by Herbert Spencer, however, that hæmorrhage into the grey matter of the spinal cord in children dying at birth or soon after delivery is not uncommon, and it is reasonable to suppose that in some of such cases which survive the paralysis may be due to hæmorrhage into the grey matter of the cord, and Boyer [84] has proved that such was the case in one instance.

The clinical evidence which is here brought forward in support of intra-uterine poliomyelitis is admittedly open to question, in that it is based on the statement of the mother of the child and not on personal observation, but the pathological evidence is complete.

The question of poliomyelitis occurring during intra-uterine life was discussed in a paper published in BRAIN, 1910 [81], and the case in which the diagnosis was made is there fully reported with a pathological examination proving that the condition was one of poliomyelitis.

Another case of poliomyelitis of the right arm and left leg occurring during intra-uterine life has since come under my observation, but no further pathological proof has been obtained :—

A. S., the second of three children, was born in September, 1911. The mother was not attended by a doctor. The mother states that she did not notice the weakness of the right arm until the child was 2 months old, but this child, unlike her other children, never made any attempt to move its arm. Wasting of the left leg was noticed some months later, but no attention was paid to this until the child was 18 months old, when it was found that it could not walk. The child had no acute illness from the time of birth till 2 months old, when the paralysis was first remarked. The birth was easy, and there is no evidence of injury during parturition. The child is intelligent and well nourished, has a complete flaccid palsy of the right arm, with considerable wasting, and a flaccid palsy of the left leg, also accompanied by wasting. The knee-jerk on the right side is active, on the left side absent. The child presents

the typical features of a case of poliomyelitis. The question which arises is whether this condition occurred during intra-uterine life, at birth, or subsequently. It seems impossible, considering the severity and wide extent of the lesion, that the child could have had an acute attack of poliomyelitis which should have escaped the mother's attention between birth and the second month of life. The paralysis of the right arm and the left leg is not such as one would expect from a birth injury. The case is clinically very similar to that already recorded, in which the *post-mortem* showed changes in the spinal cord characteristic of old poliomyelitis.

A third case with complete flaccid palsy of the neck muscles came under my observation in which the weakness had been present from the time of birth, the child dying when aged 2 years. No pathological examination was permitted. Further evidence on this subject is required.

(5) *Herpes Zoster in relation to Poliomyelitis.*

It is well recognized that herpes occurs not only in association with a localized paralysis in the same individual, but is also liable to be present in an epidemic form at the same time of year and in the same locality as poliomyelitis.

Garrow [124] described such a prevalence in the epidemic on the west coast of Cumberland in 1910. Brincker [120], in his report on the Stepney prevalence in 1914, states that herpes zoster was also prevalent at the same time. Many examples of herpes zoster of the forehead and face in association with ocular paralysis are on record, others of cervical herpes with facial paralysis, others of trunk or limb herpes with trunk or limb paralysis.

It is quite certain that many of these cannot be attributed to the virus of poliomyelitis ; some may be vascular, as Farquhar Buzzard [123] suggests, others are probably syphilitic, as in the case recorded by Parkes Weber [117], but there are others with an acute and sudden onset which might be attributed to poliomyelitis ; and Ramsey Hunt [127] has described acute posterior poliomyelitis of the geniculate and neighbouring ganglia.

Stanley Barnes [119] has described in considerable detail a case of right facial paralysis with herpes in the distribution of the third and fourth cervical on the same side in a man, aged 40, who recovered completely.

Alex Bruce [122] described a case of herpes of the seventh and eighth intercostal spaces, associated with weakness of the limb on the same side, with a dissociated form of anæsthesia ; he hypothesized a lesion at the base of the posterior horn which may give rise to such a group

of symptoms, involving the fibres of the pyramid as they pass from that structure to the anterior horn cells.

Frederick Taylor [128] recorded in 1895 a case of shingles followed by paralysis of the abdominal muscles in a man, aged 60. The paralysis of the muscles was first noticed about three weeks after the appearance of the rash. Three years later the paralysis was still present. He mentions similar cases recorded by Broadbent and Joffroy.

Further, Head and Campbell [126] have shown pathologically that the changes in the posterior root ganglia producing herpes are similar to those found in poliomyelitis.

Griffon [125] examined the cerebrospinal fluid in eleven cases of herpes zoster and found more or less marked lymphocytosis in all. It is a striking fact that nearly all the recorded cases of paralysis associated with herpes are in adults, and in many cases in elderly people.

In childhood the simultaneous occurrence of herpes zoster with poliomyelitis is rare, and the following is one of the few cases I have seen in childhood:—

A. R., aged 7, was taken ill with "influenza" in December, 1914. He had great pain in the right shoulder and a rash over the right side of the chest. When first seen, six weeks after the onset, there were marked weakness of the shoulder muscles and the remains of the rash over the thorax, indicated by pigmentation and slight thickening of the skin. The rash cleared up entirely, but a permanent weakness of the right shoulder remained.

A rash sometimes accompanies poliomyelitis, formed of small vesicles, widely distributed over the trunk and limbs, mostly on the former. Brown [121], in Toronto, described a small, shotty papule with a tiny inflammatory base which might or might not go on to vesiculation in association with poliomyelitis. If it did, the vesicle resembled a small chicken-pock, containing clear fluid.

Association of Herpes Zoster with a Generalized Eruption of Varicella-like Spots.—Many cases of herpes zoster associated with, or followed by, a generalized vesicular eruption have been described. These have recently been collected by Parkes Weber [118], who records a case of oculo-motor paresis and herpes associated with a generalized eruption.

It has been suggested that herpes zoster is a modified and localized form of varicella, and Johann von Bokay published nine observations in support of this view, and other writers quote similar cases. Weber discusses but does not favour this view. Whatever the pathology may be, the important clinical observations remain, that cases of herpes

zoster and a diffuse eruption like varicella occur associated with a localized paralysis of muscles in the same individual.

That some of these cases may be due to the virus of poliomyelitis is possible, but from the fact that the herpes commonly precedes the paralysis, and that the larger proportion of the cases is seen in persons of advanced years, it seems that toxic agents other than poliomyelitis must play an important part in the production of the associated symptoms. It is in cases of this nature that some simple serum test would be of such diagnostic value.

(6) *Cerebrospinal Fluid in Poliomyelitis.*

The examination of the cerebrospinal fluid in cases of poliomyelitis has yielded variable results. In some cases the fluid has been normal, in others there has been an excess of albumin, with a moderate increase of lymphocytes, in others again a very large increase of these cells.

The condition of the cerebrospinal fluid has varied not only with the time after the onset of symptoms at which the fluid was examined, but also with the nature of the case, the cases with the most marked meningeal symptoms tending to yield the largest cell count. Netter states that in the early stages of poliomyelitis the cerebrospinal fluid is definitely fibrinous and rich in cells, many of which may be polymorphonuclear.

Gay and Lucas [94] have studied the cerebrospinal fluid in monkeys during the incubation, the prodromal, and the acute stages of the disease, and in *eleven human* cases in the pre-paralytic stages. In these eleven cases the cell count varied from 55 to 580 per cubic millimetre, and the percentage of mononuclears from 75 to 100.

Peabody, Draper, and Dochez [107] examined 233 fluids from sixty-nine cases. The number of cases seen in the first week (dating from onset of symptoms and not of paralysis) was forty-three; in the second week, forty-five; in the third week, forty; in the fourth week, thirty. Four cases were seen in the pre-paralytic stage, and two in abortive cases.

The examination of the cerebrospinal fluid included pressure, number of cells per cubic millimetre, types of cell, chloride, reduction of Fehling, and globulin contents. Almost all the fluids were clear, only a few showed any opalescence. A web-like clot was seen in a small proportion of cases and in the early stages of the disease. It bore no relation to the globulin content. The pressure was usually somewhat above the normal, but the observations were unsatisfactory owing to variation due to respiratory efforts or crying. Chlorides were present in normal amount. Every fluid showed the normal reduction of Fehling solution.

The type of cell is almost always mononuclear early in the disease, but in the pre-paralytic period the polymorphonuclears may amount to 80 to 90 per cent. of the total.

The commonest type of fluid seen in the whole series is one with a normal or slightly increased cell count and a well-marked globulin reaction. Two other types are seen: (1) with a high cell count and a normal or very slight globulin reaction; (2) a fluid with a normal or low cell count and a very marked globulin reaction. Twenty-six cases showed a slight globulin reaction and a cell count of 50 or over.

The following conclusions are deduced: fluids taken during the early days of the disease, and especially before the onset of paralysis, tend to show an increased cell count with a low or normal globulin content; in the early stage the polymorphonuclear cells may amount to 90 per cent. of the total; most fluids, however, show almost exclusively lymphocytic and large mononuclear cells. After the first two weeks the cell count drops to normal, and there is frequently an increase in the globulin content. A slight increase in the globulin may persist for seven weeks or longer. Analogous changes may be found in the fluid of abortive cases. All fluids examined reduced Fehling's solution.

Experience drawn from a series of cases in which the cytological examination was made by Dr. Forbes and Dr. Nabarro, at the Children's Hospital, mostly two to three weeks after the onset, would indicate that at that period the cerebrospinal fluid had in most cases returned to the normal. Even in the acute cases the increase in the number of lymphocytes has been small, as has also been the amount of albumin.

Forbes, [91], in a series of thirty-three specimens from thirty cases of [illegible]omyelitis, examined at periods of from three days to six weeks after the onset, found in twenty-four specimens the fluid was clear and free from clot. In eight trace of blood was present. In one specimen a very fine web formed on standing.

Cytological examination showed the presence of lymphocytes slightly in excess of the normal (1 to 5 per cubic millimetre), but in six specimens there was a definite increase above the normal, and in another six no cells, or only the normal few cells were present.

Netter points out that it is in the meningeal type of the disease that the cerebrospinal fluid shows most changes, and he noted that in some epidemics the meningeal type may form a considerable proportion of the cases; he quotes instances of 50 per cent. and over.

The meningeal type must, I think, be rare in England. Of cases

seen during the year 1915 at the Children's Hospital, only two presented symptoms suggestive of meningitis. One died and the other recovered.

The diagnostic value of the examination of the cerebrospinal fluid in cases presenting symptoms of cerebrospinal disease is considerable.

In the first place it separates the cases with meningeal symptoms into two large groups: (1) Those in which the cerebrospinal fluid is turbid and contains a high percentage of polymorphonuclear cells; and (2) those in which the fluid is clear or slightly cloudy, and contains an increased percentage of cells, lymphocytic in character.

The first group is due to the presence of one of the infective organisms, meningococci, pneumococci, streptococci, influenza, *typhosus* or *coli* bacilli; the second to tubercle, syphilis, poliomyelitis, mumps, sinus—thrombosis, measles, tumour, and late cases of infective meningitis.

It has been shown that rarely a case of meningococcal meningitis may, in its early stages, give a fluid which is clear and contains but few cells; such cases are rare, and in a long series of meningococcal infection I have never come across one, although I have observed such a case in the earliest stage of a pneumococcal meningitis. As has already been stated, the reverse is also true—viz., that a case of poliomyelitis may, in its earlier stages, show a high polymorphonuclear count.

The important class to consider is the second—i.e., those in which there is an increase of the lymphocytic cells.

There can be little doubt that the condition which most frequently gives rise to a lymphocytic increase in the cerebrospinal fluid is a *tuberculous meningitis*—if tubercle bacilli are found, diagnosis is certain; but with a negative return the diagnosis is still uncertain. In tuberculous meningitis the reduction of Fehling solution is usually absent or delayed, in poliomyelitis the reaction is almost always present and immediate. The percentage of globulin is variable, but is usually higher in tuberculous meningitis.

In syphilis there is a marked lymphocytosis; but the chronicity of the case, with the high globulin content, together with the positive Wassermann, render the diagnosis clear.

The experimental work of Gordon [95] and the clinical observations of Anthony Feiling [89] on cases of mumps and on a fatal illness in children associated with acute interstitial parotitis are important in this connexion, for in both a lymphocytic meningitis may be present. Gordon took washings from the mouth and saliva from ten cases

of mumps from the first to the sixth day after onset of the disease. Having passed these through a Berkefeld filter, he injected the filtrate intra-cerebrally into ten monkeys. Four of the monkeys developed meningitic symptoms, and in one the cerebrospinal fluid was found to contain 1,500 white cells per cubic millimetre, 82 per cent. with lymphocytosis, 12 per cent. polymorphonuclears. The changes found in the nervous system were infiltration of the pia-arachnoid with lymphocytes; the perivascular infiltration characteristic of poliomyelitis was absent. There was no infiltration of the grey matter.

Gordon concludes that the experiments seem to justify the view that in a proportion of cases of mumps a virus occurs in the saliva that passes through a Berkefeld filter, and is capable of producing in the monkey, by intra-cerebral injection, a lymphocytic meningitis, together with hyperæmia of the central nervous system and acute degenerative changes in a proportion of the neurons. Furthermore, if the animal lives long enough acute interstitial parotitis may be produced. Mumps is therefore probably due to an ultra-microscopic organism.

Gordon next deals with a series of twelve cases of acute and fatal illness with cerebral symptoms in children, the cerebrospinal fluid showing a marked lymphocytosis, death taking place in twenty-four hours to twelve days.

The cerebrospinal fluid in six cases was clear and showed no bacilli; in three cases there was no increase in the number of cells, whilst in two it was 446 per cubic millimetre and 6,000 per cubic millimetre respectively. After death none of the ordinary causes of meningitis was found; the central nervous system appeared congested. In all the eleven cases in which the cerebrospinal fluid was examined *post mortem*, the cells present were found to be lymphocytic. Section of the brain and spinal cord showed no infiltration of the substance, the only change being a variable amount of chromatolysis in the cells. In one case only was a perivascular infiltration found at one point in the medulla.

In eleven of the cases foci of acute interstitial inflammation were found to be present in one or more of the salivary glands.

From five of the eleven cases monkeys were inoculated intra-cerebrally with an emulsion of pieces of the parotid gland and spinal cord passed through a Berkefeld filter. The result of these experiments was negative. The nature of the virus to which the death of these children might be attributed must remain doubtful.

Feiling [89] describes a case of lymphocytic meningitis following mumps in which the cells numbered 2,500 per cubic millimetre,

lymphocytes amounting to 96 per cent. Ten days later the number of cells had fallen to 20 per cubic millimetre, and the child recovered.

Measles again may be followed by acute cerebral symptoms, and the cerebrospinal fluid may show a high lymphocytic count.

Sinus thrombosis, cerebral abscess, infective conditions in the region of the brain (mastoid disease), and cerebral tumours, when they come in close relation to the ventricles, give rise to a lymphocytic cerebrospinal fluid.

The knowledge that a serous meningitis is present may not be of great diagnostic value, but a serous meningitis of acute onset which rapidly clears up is strongly in favour of poliomyelitis.

(7) *Blood in Poliomyelitis.*

Peabody, Draper, and Dochez [107], who examined the blood of patients with poliomyelitis, found a constant and marked leucocytosis. In several instances the count has been as high as 30,000. In only one case was there a definite leucopenia. Besides the increase in the total number of cells there has been an equally constant increase of polymorphonuclears of 10 to 20 per cent.

The visceral lesion of poliomyelitis showing the active part of phagocytosis played by the polymorphonuclear cells is perhaps sufficient cause for the polymorphonuclear increase in the circulating blood.

In view of the fact, however, that the brunt of the body's attempt at defence falls upon the lymphatic system, and that the cells which are assembled at the point of attack seem to be lymphocytes, one might be led at first to expect a lymphocytosis in the blood. On the other hand, the great destruction of lymphocytes which is evident in the visceral lesions suggests that these cells are relatively few in the circulation because they are constantly being withdrawn to meet the invasion of the virus at its various points of attack. It will require a more fundamental knowledge of the kind of reaction the body develops to this type of infecting agent before a correct explanation of the blood picture can be made. At all events, while the blood picture in poliomyelitis is perhaps not any more specific than is the spinal fluid, it is helpful. If taken in connexion with other available evidence, a leucocytosis of 15,000 to 30,000 is distinctly suggestive of the disease in question, especially if the polymorphonuclear cells are increased at the expense of the lymphocytes.

Other observers have found no change or a leucopenia, and it seems probable that in most cases the changes in the blood are inconsiderable.

Few observers have had the opportunity of examining the blood in the pre-paralytic stage of the disease such as fell to the lot of Peabody, Draper and Dochez.

Chapter VII.—Treatment.

(1) *General.*

Recognizing that poliomyelitis is an acute specific fever, having an incubation period of four to twelve days, the patient should be isolated. In hospital it is not necessary to place the patient in a separate ward, and bed isolation is sufficient to prevent the chance of infection. Personally I have never seen poliomyelitis either spread or arise in the ward, although I know of one infant who had been months in an institution develop the disease, there being no other cases in the ward, although there were chronic cases in the hospital. Peabody, Draper and Dochez isolated their patients in separate wards and dealt with them in the same way as other acute infectious diseases.

As the virus is known to exist in the nasal and buccal mucous membrane, it is well to pay careful attention to these and to any discharge therefrom, and to clean the nose and mouth two or three times a day with a 0·2 per cent. solution of permanganate of potash or chlorine water.

The acute stage is often attended by fever, sometimes by convulsions and pain, with rigidity of the neck and spine. Pain may be intense, sometimes so severe that the patient dreads the least touch of the bed or bed-clothes, or movement of the affected limbs. At times the patient may be unconscious, following a convulsion, with marked head retraction, opisthotonos, and signs of meningitis. As has been pointed out, the diagnosis in such cases depends upon the examination of the cerebrospinal fluid. Sometimes, owing to the rigidity of the back, it may be difficult, if not impossible, to do a lumbar puncture, and in order to perform this it is necessary to administer an anæsthetic. Lumbar puncture by itself often seems to relieve the most acute symptoms. It therefore is useful not only as a method of diagnosis, but also as a means of treatment.

(2) *Serum Treatment.*

It has been shown experimentally that immune serum has no power to prevent the development of the disease when injected simultaneously, or after the virus has been injected; Flexner and Amoss [132] have

shown that the intrathecal injections of an immune serum are effective when introduced in the pre-paralytic stage in delaying and preventing poliomyelitic infection in the monkey. This method of intraspinal injection of immune serum has been used with success by Netter [136] in cases of poliomyelitis of the acute ascending variety. In one case eight injections were given of from 4 c.c. to 12 c.c., obtained from a series of old cases of poliomyelitis.

The method is as follows: some 20 c.c. to 30 c.c. or more of blood are obtained by venupuncture from a patient who has passed through an attack of poliomyelitis (the length of time after the attack is not important, for it has been shown that the blood preserves its antitoxic properties for several years). The serum is separated by allowing the blood to clot and by centrifugalization. The serum is warmed to 98° F. Lumbar puncture is performed on the patient and an amount of cerebro-spinal fluid removed corresponding to that of the serum which it is proposed to inject—usually about 10 c.c. The serum is now slowly injected and the bed of the patient tilted so as to allow it to gravitate cerebral-wards. The injection can be repeated daily from three to four days or more.

There is little or no difficulty in carrying out the treatment. The difficulty is to obtain an old case of poliomyelitis who has already been tested and given a negative Wassermann reaction, and who is willing to give the necessary blood at the same time as a suitable case of acute poliomyelitis presents itself for treatment.

It is useless to carry out this treatment when the disease has already become quiescent, and the typical cases for such are either—(1) presenting symptoms of an ascending or progressive poliomyelitis, or (2) presenting meningeal symptoms, or (3) (if the diagnosis can be made) in the pre-paralytic stage.

I have on two occasions carried out the treatment: once in a baby with a lymphocytic meningitis; the child recovered, but with considerable mental defect. The second was a case of widespread and extending poliomyelitis under the care of my colleague, Dr. Still. This child, I am informed by Dr. Sidney Smith, made an almost complete recovery, but that cannot necessarily be attributed to the serum.

This method of treatment can be effective in a very limited group of cases only during the acutest stage, and special circumstances are needed for carrying it out—i.e., a suitable giver and laboratory facilities.

The possibility of employing the sera of animals has been considered. Flexner and Lewis found that the sera of horses and rabbits had no

viricidal action. Sheep's serum was slightly active and might be increased by injections of the virus, but the degree of activity appears to have been small.

(3) *Drugs.*

The acute pain associated with the disease can to a large extent be relieved by careful support of the limbs and of the patient, and of the arrangement of the bed. Aceto-salicylic acid is the drug which in my experience gives most relief; other coal-tar derivatives are of value, but in some cases morphia is needed. The administration of hexamine has been advocated on experimental grounds, for it has been shown that it passes into the cerebrospinal fluid, and that in animals it tends to delay, if it does not prevent, infection of the spinal cord by pathogenic organisms. It should be administered in large doses, 10 gr. every four hours to young children. There is no doubt that hexamine reaches the spinal fluid, but there is some doubt that it is present in that fluid in the active form of formaldehyde or that it has any beneficial effect. The only disadvantage in the administration of this drug is that it occasionally gives rise to hæmaturia.

(4) *Rest, Posture, Re-education.*

There can be no doubt that rest is the most important method of treatment. The too early movement may in some cases restart the disease which has become quiescent, and relapses have been produced in this way. A child with an acute attack of poliomyelitis should be kept absolutely at rest in bed for at least three weeks; the length of time necessarily depends on the severity, but even in the slightest cases movement before this time is inadvisable. Though bed may give rest to the body generally, it does not necessarily afford the complete physiological rest required for recovery of a muscle, and hence it is essential to consider the principles on which such rest can be secured. Sherrington [138] has shown that the normal skeletal muscle is possessed of a degree of tension or tone, and that there is a reciprocal innervation of muscles, so that when the flexor contracts there is an active relaxation or inhibition of tone in the extensors. The tone of the muscles is largely dependent on afferent impulses. If the extensors are paralysed and the limb lies in the flexed position, there is a tendency for the extensor to become stretched, whilst the flexor becomes more contracted; but not only is there an actual stretching of the paralysed muscle, but there is in all probability an active inhibition giving rise to a further loss of tone. The anatomist, William Mackenzie, expresses

the same in somewhat different language. The muscle adjustments are so fine that immediately the nerve-cell governing the action of the flexor is affected, the extensor opponent begins to over-act, and this over-action must be prevented for the following reasons: (1) It does not allow complete rest of the affected anterior horn-cell; (2) by over-stretching the affected muscle it interferes with its recovery. Robert Jones [134] expresses the same facts by a mechanical metaphor, saying: "The whole reflex apparatus by which the spinal nerve-cell and muscle react on each other to their mutual benefit is put out of gear." And he insists on relaxation of the paralysed muscle; but as William Mackenzie [135] points out, relaxation is only the beginning of treatment, and more than this is required, and that is re-education of the paralysed muscle. All are agreed that a stretched muscle is at a disadvantage and will not recover its power until relaxed.

Posture.—Posture is therefore the great factor in securing physiological rest to a muscle, and it is important to consider what is the *zero position* of any given muscle. Mackenzie defines the zero position as the position of anatomical rest in which the individual muscle itself is relaxed, and both its own action and that of its opponent's prevented. Sherrington has shown that the distribution of tonus is arranged on a plan of strict co-ordination, and that reflex tonus embraces those movements which counteract the effect of gravity, and that postural contraction can be maintained for long periods without fatigue. A position which can be maintained without fatigue must be the position of rest.

Application of the Principles of Rest, Posture, and Re-education in the Treatment of Paralysed Muscles.

Rest, posture and re-education are the important methods of treatment. Various methods have been adopted for keeping the paralysed muscles at rest and in a state of "relaxation." Simple rest in bed is regarded by some as sufficient. Others place the limbs between sandbags, so as to prevent movement and misplacement of the limb. Others place a board at the bottom of the bed, which is often effective in keeping the foot in the dorsi-flexed position. Various splints of metal and other material have been used. Some medical men have advocated placing the patient or the limb into a plaster of Paris mould, so that no movement is possible. Robert Jones insists that the paralysed muscles must be placed into the position of complete relaxation, and that any deviation from this position, even momentary, is harmful. Success

has, and will, attend all these methods, but they all have the same disadvantage that they tend to immobilize the patient for the period of many months, and give the child but little chance of physiological action and re-education of the muscles, which may have been greatly or slightly affected.

Plaster-of-Paris.—The use of plaster-of-Paris as a means of support is easy, and in selected cases of poliomyelitis is most valuable. In some the limb can be placed into plaster-of-Paris in the ordinary way; in others, a removable plaster-of-Paris splint can be made so that the limb is kept in the zero position until recovery has taken place, or until a more permanent splint is made, and treatment by massage, passive and resistance movements can be carried out in the meanwhile.

Splints.—The practical application of the above principles has been carried out by the following method: The paralysed limb or limbs are placed in a light celluloid splint accurately fitted to the limbs as soon as it is possible to make the cast after the onset of the disease. These splints were first made by M. Calot [131] in France, and introduced into this country by Gauvain [133], who employed them extensively in the treatment of tuberculous joints, and most kindly instructed me in their use [130].

It is not my intention to enter into any detail here as to their construction, but seeing that the splint is to serve in most cases not only for keeping the muscles at rest, but also as a support in walking, it is essential that the position of the limb should be such that progression is possible. The splint is moulded on a plaster-of-Paris cast of the limb, and it is the making of this cast which is important, for the limb must be in the *zero position*, or in other words, the position normally assumed to counteract the effect of gravity when the patient is in the erect position. That position, so far as the legs are concerned, is one of *slight flexion of the knee* with the *foot at right angles*, or at an angle slightly greater than a right angle to the tibia (fig. 36).

The advantages of this form of splint are: (1) That they maintain the muscles constantly in a position of rest, for they can be worn day and night; (2) they do not immobilize the patient, so that walking exercise can be carried out without the liability to produce deformity or stretching of the muscle; (3) they are easily removed and replaced, so that other methods of treatment can be carried out; (4) no special boots or shoes are required (fig. 37).

The aim of treatment has been to keep the limbs in a normal position and free from deformity whilst recovery is taking place, and

FIG. 36.—Photo of child with flaccid paralysis of both legs in celluloid splints. Note that the splint is taken sufficiently high so that the weight of the body is supported on the tuber ischii, the knee is slightly flexed and the foot is at right angles to the tibia.

FIG. 37.—Photo of same child in walking machine. The early stage of the re-education of the child in walking.

the result has to a great extent been attained. In the legs with paralysis of the muscles of the thigh and below the knees no great difficulty arises. All the mal-position of the foot and knee can be prevented. It is somewhat difficult to prevent the outward rotation and abduction of the leg below the knee in those cases in which the biceps femoris is relatively good compared to its antagonists. So long as the child has remained in the hospital no deformity has arisen, but under home conditions in which the splint is left off and massage and

FIG. 38.—Photo of same child at a later stage, when the child can walk easily and rapidly with the machine.

educative movements not maintained, the deformity readily occurs and is not easily corrected. The flexor and extensor muscles of the hip are, however, the most difficult to keep in a position of relaxation. So long as the child is lying in bed the tendency for the flexors of the hip to contract can be prevented, but if the child is allowed to sit up the flexors tend to assume a contracted position, with the result that the hip is flexed on the pelvis (fig. 29, p. 170). In such cases it is best to allow the child only to assume the erect or lying position. The erect position can usually be assumed by means of a walking machine (fig. 38), whereby

the child supports the weight of the trunk on the hands and allows the limbs to swing. Such a position tends to re-educate and bring into function not only the flexor and extensor movements of the thigh, but also all the muscles of back and abdomen. Careful attention to the extensors of the legs, with regular massage and movements, will to some extent prevent this contraction, but in severe cases, in which the extensors are completely paralysed and the flexors but little affected, the flexors come into action, and when the child attempts to assume the erect position lordosis is produced. I am rather of opinion that in these cases it is best to put the flexors out of action by division, and if this be done early it gives the opposing extensor a greater chance of recovery and prevents any displacement of the hip-joint, which is likely to occur if the contracture is of long duration.

A still more difficult condition to deal with is that of paralysis of the flexor of the hip with good power remaining in the extensor. This is fortunately a very rare manifestation. It is possible to place the child in a fixed position with the knees and thighs flexed, and this has been done and maintained for some months; but a few days after the child is taken out of plaster the position of hyper-extension is again assumed. Allusion to this form of deformity has already been made in the clinical section of these lectures, and in the case referred to treatment was completely unsuccessful (fig. 30, p. 170).

Abdominal and back muscles.—If these muscles are seriously involved, standing and walking are almost impossible. On the other hand, there is no exercise which is so effectual in re-educating them as that of attempting to balance and assume the erect position. Deformity can be prevented by the recumbent position and by extension, but should the affection of the muscles be severe the child will need artificial support to prevent deformity when it assumes the erect position.

Walking exercise and the erect position.—When once the legs are splinted it is possible to get the patient into the erect position, and such allows of the physiological use of the back, trunk and pelvic muscles. Such walking exercises are carried out by the use of a walking machine, which supports the child both physically and morally, for it is important to give the child complete confidence in itself (figs. 37, 38, 39).

Arms.—The most common form of paralysis of the arm is a paralysis of the deltoid, biceps and shoulder muscles, while the forearm remains relatively good. In order to relax the deltoid the arm must be abducted from the thorax, and it is usual to place the hand behind the head so as to secure this. I have adopted two methods in dealing with these cases:

(1) To make a celluloid splint which will hold the arm abducted and flexed (figs. 40 and 41); (2) a Fairbank splint, which keeps the arm in this position (fig. 42). The disadvantage of the former is that it is difficult to make, and the angle of the abduction cannot be altered. The advantages of the latter are that it is easy and cheap to make, and is readily adjusted to any angle required. The arm should be kept in that

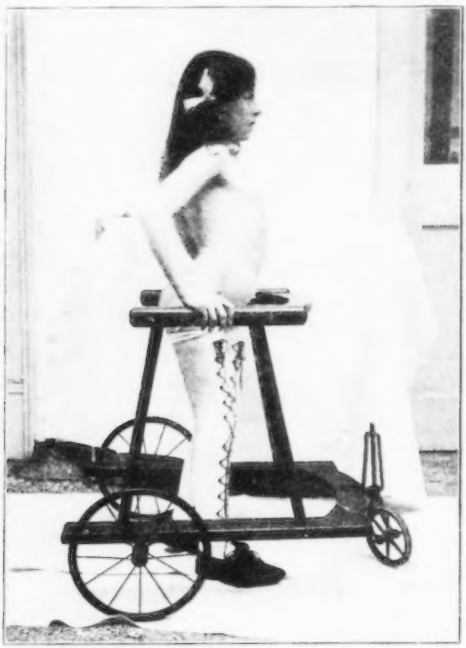


FIG. 39.—Photo of child with poliomyelitis learning to walk. Considerable lordosis has been produced owing to the long standing contraction of the flexor of the hips.

position day and night for at least twelve months. If at the end of that period no improvement has taken place it is improbable that any recovery will occur, and the arms can be placed in the flexed position at the side, so that the hand may be of greater service.

Neck.—The isolated paralysis of muscles of the neck is a somewhat rare manifestation. A child with this affection is quite unable to walk, owing to the inability to maintain the balance. A collar which will hold the head in the erect position not only places the paralysed muscles at rest in the zero position, but also prevents the head being jerked

FIG. 40.—Child with paralysis of the deltoid and biceps muscles in celluloid splint. The splints tend to keep these muscles relaxed and prevents the over-action and contraction of the latissimus dorsi and pectoral muscles.

FIG. 41.—Man with poliomyelitis of the shoulder muscles of the left arm. The splint has an additional support from a strap and band round the right shoulder.

either forward or backwards, thus throwing the child to the ground (fig. 43).

The above are simply instances of the application of the principles that the paralysed muscle must be placed in the position of rest. Almost every case varies in the muscles paralysed, and needs individual thought as to the position in which the limb should be placed. If, however, medical men will adopt the practice of placing the limb in a splint in a position of rest *at an early stage of the disease*, not only will the recovery of the muscles be more complete, but the greater portion of the deformities which one now sees as a result of poliomyelitis will be prevented.

Re-education of movements and muscles.—The re-education of the paralysed muscle is of great importance. With a severely paralysed muscle it is essential in early stages to place the limb in such a position that the load on the muscle is at its minimum; for the sake of example, with a paralysed biceps of the arm the upper arm must be in the horizontal position, as it is when the patient is recumbent, the forearm in the vertical position at right angles. Only a very small force is now required to overcome gravity and flex the arm. The angle is slowly increased and graduated to the power of the muscle as it slowly recovers. A bath is an excellent place to practise the re-education of muscles, for the weight of the limb is supported and ranges of movement are possible which are impossible without the support of the water. Education will gradually increase these movements.

(5) *Massage.*

In massage—and under this heading I include all active and passive and re-education movements—we have most valuable methods of maintaining the nutrition of the muscles and assisting recovery whilst regeneration of the damaged neurons is taking place. Friction and warmth to the skin stimulate, and are of great service in maintaining the circulation.

Warm baths and douches.—Warm baths and douches have the same effect, and are of service in relieving pain and allowing of movement in an otherwise painful joint.

(6) *Electricity.*

All forms of electricity have been employed in dealing with cases of poliomyelitis: some may be of service, others are useless, others again are harmful. It is probable that the galvanic current is of service

FIG. 42.—Child with poliomyelitis of the right deltoid and bicep in Fairbank splint. The advantage of this splint over the celluloid is that the angles can be easily adjusted.

FIG. 43.—Boy with flaccid paralysis of neck muscles in celluloid collar.

in stimulating paralysed muscles to contract, but the current, when sufficiently strong to cause a paralysed muscle to contract, gives considerable pain to children and is ill borne, and the advantages gained by no means compensate for the emotional disturbance produced.

Faradism and the alternating currents may be said in most cases to be directly harmful. They cause the active contraction of unparalysed muscles, whilst the paralysed muscles do not react; thus the paralysed muscles are stretched.

The skin stimulation to which other forms of electricity give rise may be of some benefit.

(7) *Other Methods of Treatment.*

It is not my purpose to deal with the later stages of paralyses which require some mechanical replacement of and support for the paralysed muscle, nor with the surgical aspect of the treatment of the late effects of poliomyelitis by tendon lengthening, tendon transplantation, tendon fixation, artificial ligaments, nerve-grafting, arthrodesis, and the like; but I am convinced that if the line of treatment above advocated is extensively adopted, recovery of power in the muscle will be greater and a large proportion of the deformities which are now seen in cases of poliomyelitis will be prevented.

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